

SEARCH REQUEST FORM

Requestor's Name: Jeffrey E. Russel Serial Number: 09/674,526
 Date: 3-24-2004 Phone: 571-272-0969 Art Unit: 1654
 REM 3012/6 (60) SD11 (mailbox)

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search the sequences GGFG and GGGF in STN. Please set the sequence length at SOL-4. If necessary, please use the keywords conjugate, link, carrier.

Thank you
 JER

STAFF USE ONLY

Point of Contact:
 Alexandra Wacławiw
 Technical Info. Specialist
 CM: 6A02 Tel: 308-4401
 Date completed: 3-25-04
 Searcher: Don 1A71 2-2534
 Terminal time: _____
 Elapsed time: _____
 CPU time: _____
 Total time: _____
 Number of Searches: _____
 Number of Databases: _____

Search Site

☐ STIC
☒ CM-1
☐ Pre-S

Type of Search

☐ N.A. Sequence
☐ A.A. Sequence
☐ Structure

Vendors

☐ IG
☒ STN
☐ Dialog
☐ APS
☐ Geninfo
☐ SDC
☐ DARC/Questel

POP 6
 10
 5
 15

Russel 09/674,526

=> d his

FILE 'REGISTRY' ENTERED AT 08:28:54 ON 25 MAR 2004
ACT RUSSEL/A

L1 49145 SEA FILE=REGISTRY ABB=ON PLU=ON GGFG|GGGF/SQSP
L2 138 S L1 AND SQL=4

FILE 'CAPLUS' ENTERED AT 08:30:01 ON 25 MAR 2004
L3 71 S L2
L4 32 S L3 AND (CONJUGAT? OR LINK? OR CARRIER?)
SELECT RN L4 1-32 HIT

=> fil reg

FILE 'REGISTRY' ENTERED AT 08:31:21 ON 25 MAR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 24 MAR 2004 HIGHEST RN 667234-34-6
DICTIONARY FILE UPDATES: 24 MAR 2004 HIGHEST RN 667234-34-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d que l2

L1 49145 SEA FILE=REGISTRY ABB=ON PLU=ON GGFG|GGGF/SQSP
L2 138 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=4

=> fil caplus

FILE 'CAPLUS' ENTERED AT 08:31:26 ON 25 MAR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

L) sea search
4 aa length

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN. Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is

Russel 09/674,526

strictly prohibited.

FILE COVERS 1907 - 25 Mar 2004 VOL 140 ISS 13
FILE LAST UPDATED: 24 Mar 2004 (20040324/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos l4

L1 49145 SEA FILE=REGISTRY ABB=ON PLU=ON GGFG|GGGF/SQSP
L2 138 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=4
L3 71 SEA FILE=CAPLUS ABB=ON PLU=ON L2
L4 32 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND (CONJUGAT?/OBI OR
LINK?/OBI OR CARRIER?/OBI)

=> => d que l4

L1 49145 SEA FILE=REGISTRY ABB=ON PLU=ON GGFG|GGGF/SQSP
L2 138 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND SQL=4
L3 71 SEA FILE=CAPLUS ABB=ON PLU=ON L2
L4 32 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND (CONJUGAT?/OBI OR
LINK?/OBI OR CARRIER?/OBI)

=> d .ca l4 1-32

L4 ANSWER 1 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:434299 CAPLUS

DOCUMENT NUMBER: 139:30773

TITLE: Peptides that bind to p185, and methods for the
treatment and diagnosis of tumors

INVENTOR(S): Greene, Mark I.; Murali, Ramachandran; Berezov, Alan

PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA

SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045309	A2	20030605	WO 2002-US37390	20021121
WO 2003045309	A3	20031218		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

US 2003148932 A1 20030807 US 2002-301499 20021121

PRIORITY APPLN. INFO.: US 2001-331935P P 20011121

OTHER SOURCE(S): MARPAT 139:30773

AB Peptides and pharmaceutical compns. comprising them are disclosed.
Conjugated peptides linked to detectable agents and/or cytotoxic agents.

are disclosed. A method of detecting tumors that have cell-surface p185 is disclosed. Methods of preventing transformation of a normal cell into a tumor cell in an individual at risk of developing a tumor having tumor cells which have p185 on their surfaces are disclosed. Methods of treating an individual who has cancer characterized by tumor cells that have a p185 on their cell surfaces are disclosed.

- IC ICM A61K
- CC 1-6 (Pharmacology)
Section cross-reference(s): 8, 14, 63
- IT Cytotoxic agents
(and detectable agents, peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)
- IT Chelating agents
 Linking agents
 (chelating **linker**; peptides binding to p185 for treatment and diagnosis of tumors)
- IT Toxins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (**conjugates**, with peptides; peptides binding to p185 for treatment and diagnosis of tumors)
- IT Peptides, biological studies
 RL: DGN (Diagnostic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (**conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)
- IT Radionuclides, biological studies
 RL: DGN (Diagnostic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)
- IT 67-43-6, DTPA 60239-18-1, DOTA
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (chelating **linker**; peptides binding to p185 for treatment and diagnosis of tumors)
- IT 14133-76-7, Technetium-99, biological studies
 RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
 (metastable, peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)
- IT 10098-91-6, Yttrium-90, biological studies 13981-56-1, Fluorine-18, biological studies
 RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
 (peptide **conjugates**; peptides binding to p185 for treatment and diagnosis of tumors)
- IT 241813-38-7 359887-31-3 359887-32-4 359887-36-8 359887-38-0
 359887-40-4 359887-42-6 359887-44-8 535959-77-4 535959-78-5
 535959-79-6 535959-80-9 535959-81-0 535959-82-1 535959-83-2
 535959-84-3 535959-85-4 535959-86-5 535959-87-6 535959-88-7
 535959-89-8 535959-90-1 535959-91-2 535959-92-3 535959-93-4
 535959-94-5 535959-95-6 535959-96-7 535959-99-0D, **conjugates**
 with detectable or cytotoxic agents 535960-00-0D, **conjugates**
 with detectable or cytotoxic agents 535960-01-1D, **conjugates**
 with detectable or cytotoxic agents 535960-02-2D, **conjugates**
 with detectable or cytotoxic agents 535960-03-3D, **conjugates**
 with detectable or cytotoxic agents 535960-04-4D, **conjugates**
 with detectable or cytotoxic agents 535960-05-5D, **conjugates**
 with detectable or cytotoxic agents 535960-06-6D, **conjugates**
 RL: DGN (Diagnostic use); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptides binding to p185 for treatment and diagnosis of tumors)

IT 5550-81-2 75853-32-6 403700-66-3 540490-74-2 540490-75-3

540490-76-4 540490-77-5 540490-78-6 540490-79-7 540490-80-0

540490-81-1 540490-82-2 540490-83-3 540490-84-4 540490-85-5

540490-86-6 540490-87-7 540490-88-8 540490-89-9 540490-90-2

540490-91-3 540490-92-4 540490-93-5 540490-94-6 540490-95-7

540490-96-8 540490-97-9 540490-98-0 540490-99-1 540491-00-7

540491-01-8 540491-02-9 540491-03-0 540491-04-1 540491-05-2

540491-06-3 540491-07-4 540491-08-5 540491-09-6 540491-10-9

540491-11-0 540491-12-1 540491-13-2 540491-14-3 540491-15-4

540491-16-5 540491-17-6 540491-18-7 540491-19-8 540491-20-1

540491-21-2 540491-22-3 540491-23-4 540491-24-5

RL: PRP (Properties)

(unclaimed sequence; peptides that bind to p185, and methods for the treatment and diagnosis of tumors)

L4 ANSWER 2 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:154283 CAPLUS

DOCUMENT NUMBER: 138:198591

TITLE: Polysaccharide-camptothecin derivative

conjugates for inhibiting the metastasis or preventing the recurrence of malignant tumor

INVENTOR(S): Kawaguchi, Takayuki; Okuno, Satoshi; Yano, Toshiro

PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015826	A1	20030227	WO 2002-JP8309	20020816
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				

JP 2003137818 A2 20030514 JP 2002-239094 20020820

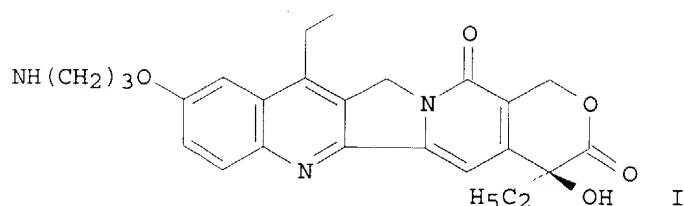
US 2003092608 A1 20030515 US 2002-224475 20020821

PRIORITY APPLN. INFO.: JP 2001-249717 A 20010821

US 2001-331255P P 20011113

OTHER SOURCE(S): MARPAT 138:198591

GI



- AB A pharmaceutical composition for inhibiting the metastasis or preventing the recurrence of a malignant tumor, which comprises as the active ingredient a polysaccharide derivative comprises a polysaccharide having a carboxyl group bound to an active substance having an antitumor activity via an amino acid or a peptide consisting of 2 to 8 amino acids which are the same or different, or a salt thereof. Preferred active substances are camptothecin derivs. I was prepared and exhibited excellent activity of prolonging lifetime in M5076 liver metastatic models.
- IC ICM A61K047-48
ICS A61P035-04
- CC 1-6 (Pharmacology)
Section cross-reference(s): 26, 33, 34
- ST polysaccharide camptothecin deriv **conjugate** antitumor
- IT Neoplasm
(metastasis; polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)
- IT Antitumor agents
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)
- IT 9004-54-0, Dextran, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(polyalc.; polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)
- IT 187803-34-5DP, **conjugate** with carboxymethyl dextran
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)
- IT 9044-05-7D, Carboxymethyl dextran, **conjugate** with taxol and camptothecin derivs. 28320-73-2 39422-83-8, Carboxymethyl dextran sodium salt 187794-49-6 288247-87-0 499982-21-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)
- IT 144008-87-7P 187794-70-3P 499982-17-1P 499982-19-3P
499982-23-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)
- IT 223537-08-4P 223537-10-8DP, **conjugate** with polyalc. carboxymethyl dextran 499982-18-2DP, **conjugate** with carboxymethyl dextran 499982-20-6DP, **conjugate** with carboxymethyl dextran
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polysaccharide-camptothecin derivative **conjugates** for inhibiting the metastasis or preventing the recurrence of malignant tumor)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:94089 CAPLUS
 DOCUMENT NUMBER: 138:158804
 TITLE: Optimized prodrugs as DDS for targeting to tumors
 INVENTOR(S): Inoue, Kazuhiro; Kuga, Hiroshi; Kumasawa, Eiji; Shiose, Yoshinobu; Ousu, Satoru; Oki, Hitoshi
 PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003034653	A2	20030207	JP 2001-250877	20010717
PRIORITY APPLN. INFO.:			JP 2001-250877	20010717
AB	The prodrugs comprising carriers, peptide spacers, and drugs, e.g. antitumor agents, analgesics, inflammation inhibitors, etc., show neither long-term in vivo accumulation nor immunogenicity, and are selectively accumulated in tumors based on EPR (enhanced permeability and retention) and released upon cleavage in the spacer part by peptidase. The prodrugs have significantly broadened therapeutic range and the carriers cleaved from the prodrugs have proper excretion property. The carriers are preferably derived from carboxymethyl dextran polyalc., which show improved flexibility of mol. chain, increased hydrophilicity, and stealth property, i.e. ability to escape recognition by macrophages. Conjugates of carboxymethyl dextran polyol with amide of (1S,9S)-1-amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13(9H,15H)-dione with Gly-Gly-Phe-Gly was prepared, and tissue distribution and antitumor effect of the prodrug were determined in mice.			
IC	ICM A61K045-00			
CC	ICS A61K031-4741; A61K031-704; A61K047-36; A61K047-48; A61P035-00			
ST	63-6 (Pharmaceuticals)			
IT	carboxymethyl dextran polyol carrier tumor targeting DDS; tetrapeptide spacer optimization antitumor prodrug; doxorubicin prodrug carboxymethyl dextran polyol carrier peptide spacer			
IT	Drug delivery systems (carriers ; optimized DDS for targeting to tumors comprising carriers such as carboxymethyl dextran polyols, peptide spacers, and drug)			
IT	Analgesics Anti-inflammatory agents Antitumor agents Drug delivery systems (optimized DDS for targeting to tumors comprising carriers such as carboxymethyl dextran polyols, peptide spacers, and drug)			
IT	Drug delivery systems (prodrugs; optimized DDS for targeting to tumors comprising carriers such as carboxymethyl dextran polyols, peptide spacers, and drug)			
IT	Neoplasm (targeting of; optimized DDS for targeting to tumors comprising			

carriers such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT Inflammation
Pain
(treatment of; optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT 200427-88-9DP, reaction products with drugs and carboxymethyl dextran polyols
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(optimized DDS for targeting to tumors comprising **carriers** such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT 4905-26-4D, reaction products with drugs and carboxymethyl dextran polyols
9044-05-7D, Carboxymethyl dextran, oxidative cleavage products, amides with doxorubicin tetrapeptide derivs. 9044-05-7D, Carboxymethyl dextran, reaction products with tetrapeptide derivs. of antitumor agents
23214-92-8, Doxorubicin 60254-83-3D, reaction products with drugs and carboxymethyl dextran polyols 61370-88-5D, reaction products with drugs and carboxymethyl dextran polyols 61430-18-0D, reaction products with drugs and carboxymethyl dextran polyols 81466-43-5D, reaction products with drugs and carboxymethyl dextran polyols 87743-02-0D, reaction products with drugs and carboxymethyl dextran polyols 105468-17-5D, reaction products with drugs and carboxymethyl dextran polyols 107889-44-1D, reaction products with drugs and carboxymethyl dextran polyols 145903-95-3D, reaction products with drugs and carboxymethyl dextran polyols 154485-92-4D, reaction products with drugs and carboxymethyl dextran polyols 154485-95-7D, reaction products with drugs and carboxymethyl dextran polyols 171335-80-1 203381-63-9D, reaction products with drugs and carboxymethyl dextran polyols 223537-10-8D, reaction products with carboxymethyl dextran 289625-27-0D, reaction products with drugs and carboxymethyl dextran polyols 395070-80-1D, reaction products with drugs and carboxymethyl dextran polyols 402751-87-5D, reaction products with drugs and carboxymethyl dextran polyols 494834-91-2D, reaction products with drugs and carboxymethyl dextran polyols 494834-92-3D, reaction products with drugs and carboxymethyl dextran polyols 494834-93-4D, reaction products with drugs and carboxymethyl dextran polyols 494834-94-5D, reaction products with drugs and carboxymethyl dextran polyols 494834-95-6D, reaction products with drugs and carboxymethyl dextran polyols 494834-96-7D, reaction products with drugs and carboxymethyl dextran polyols 494834-97-8D, reaction products with drugs and carboxymethyl dextran polyols 494834-98-9D, reaction products with drugs and carboxymethyl dextran polyols 494834-99-0D, reaction products with drugs and carboxymethyl dextran polyols 494835-00-6D, reaction products with drugs and carboxymethyl dextran polyols 494835-01-7D, reaction products with drugs and carboxymethyl dextran polyols 494835-02-8D, reaction products with drugs and carboxymethyl dextran polyols 494835-03-9D, reaction products with drugs and carboxymethyl dextran polyols 494835-04-0D, reaction products with drugs and carboxymethyl dextran polyols 494835-05-1D, reaction products with drugs and carboxymethyl dextran polyols 494835-06-2D, reaction products with drugs and carboxymethyl dextran polyols 494835-07-3D, reaction products with drugs and carboxymethyl dextran polyols 494835-08-4D, reaction products with drugs and carboxymethyl dextran polyols 494835-09-5D, reaction products with drugs and carboxymethyl dextran polyols 494835-10-8D, reaction products with drugs and carboxymethyl dextran polyols 494835-11-9D, reaction products with drugs and carboxymethyl dextran polyols 494835-12-0D, reaction products with drugs and carboxymethyl dextran polyols 494835-13-1D,

reaction products with drugs and carboxymethyl dextran polyols
 494835-14-2D, reaction products with drugs and carboxymethyl dextran
 polyols 494835-15-3D, reaction products with drugs and carboxymethyl
 dextran polyols 494835-16-4D, reaction products with drugs and
 carboxymethyl dextran polyols 494835-17-5D, reaction products with drugs
 and carboxymethyl dextran polyols 494835-18-6D, reaction products with
 drugs and carboxymethyl dextran polyols 494835-19-7D, reaction products
 with drugs and carboxymethyl dextran polyols 494835-20-0D, reaction
 products with drugs and carboxymethyl dextran polyols 494835-21-1D,
 reaction products with drugs and carboxymethyl dextran polyols
 494835-22-2D, reaction products with drugs and carboxymethyl dextran
 polyols 494835-23-3D, reaction products with drugs and carboxymethyl
 dextran polyols 494835-24-4D, reaction products with drugs and
 carboxymethyl dextran polyols 494835-25-5D, reaction products with drugs
 and carboxymethyl dextran polyols 494835-26-6D, reaction products with
 drugs and carboxymethyl dextran polyols 494835-27-7D, reaction products
 with drugs and carboxymethyl dextran polyols 494835-28-8D, reaction
 products with drugs and carboxymethyl dextran polyols 494835-29-9D,
 reaction products with drugs and carboxymethyl dextran polyols
 494835-30-2D, amides with carboxymethyl dextran oxidative cleavage
 products

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (optimized DDS for targeting to tumors comprising **carriers**
 such as carboxymethyl dextran polyols, peptide spacers, and drug)

IT 20234-78-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (reaction products with antitumor agents and carboxymethyl dextran
 polyols and; optimized DDS for targeting to tumors comprising
carriers such as carboxymethyl dextran polyols, peptide
 spacers, and drug)

IT 9031-96-3, Peptidase

RL: CAT (Catalyst use); THU (Therapeutic use); BIOL (Biological study);
 USES (Uses)
 (spacer cleavage by; optimized DDS for targeting to tumors comprising
carriers such as carboxymethyl dextran polyols, peptide
 spacers, and drug)

L4 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:849477 CAPLUS

DOCUMENT NUMBER: 137:348514

TITLE: High throughput screening methods using magnetic
 resonance imaging agents

INVENTOR(S): Meade, Thomas J.

PATENT ASSIGNEE(S): Metaprobe, Inc., USA

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087632	A1	20021107	WO 2002-US14194	20020502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002197648 A1 20021226 US 2002-139145 20020502

PRIORITY APPLN. INFO.:

US 2001-288963P P 20010502

AB The invention relates to a wide variety of different methods and compns. that find use in high throughput screening applications utilizing magnetic resonance imaging (MRI) contrast agents. The invention provides a library of MRI contrast agents comprising a chelate, a paramagnetic metal ion, and a different candidate agent. The candidate agent may be covalently attached to the chelate, or indirectly attached to the chelate via a linker. Suitable candidate agents include peptides, carbohydrates, nucleic acids and lipids. The methods may be applicable for screening for protease-activated MRI contrast agents, for screening of animals pretreated with a drug candidate, for screening of transgenic animals, for imaging gene expression, for imaging disease progression, etc.

IC ICM A61K051-00

ICS A61M036-14

CC 8-1 (Radiation Biochemistry)

Section cross-reference(s): 1, 9, 14, 63

IT Carbohydrates, biological studies

Lipids, biological studies

Nucleic acids

Peptides, biological studies

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(gadolinium-complexed **conjugates**; high throughput screening methods using magnetic resonance imaging agents)

IT **Linking agents**

Photolysis

(high throughput screening methods using magnetic resonance imaging agents with photocleavable **linkers**)

IT 57-22-7D, Vincristine, gadolinium-complexed **conjugates**

865-21-4D, Vinblastine, gadolinium-complexed **conjugates**

7440-54-2D, Gadolinium, **conjugated** complexes 23214-92-8D,

Doxorubicin, gadolinium-complexed **conjugates** 29767-20-2D,

Vm-26, gadolinium-complexed **conjugates** 33069-62-4D,

Paclitaxel, gadolinium-complexed **conjugates** 33419-42-0D,

Etoposide, gadolinium-complexed **conjugates** 53643-48-4D,

Vindesine, gadolinium-complexed **conjugates** 60239-18-1D, DOTA,

gadolinium-complexed **conjugates** 83678-67-5D, Gadolinium-DOTA,

conjugates 97682-44-5D, Irinotecan, gadolinium-complexed

conjugates 114977-28-5D, Docetaxel, gadolinium-complexed

conjugates 123948-87-8D, Topotecan, gadolinium-complexed

conjugates 474958-03-7 474958-04-8 474958-05-9 474958-06-0

474958-08-2

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(high throughput screening methods using magnetic resonance imaging agents)

IT 75853-32-6 211918-90-0 409334-94-7 409334-95-8 409334-97-0

474949-49-0 474949-51-4 474949-60-5 474949-64-9 474949-67-2

474949-72-9 474949-75-2

RL: PRP (Properties)

(unclaimed sequence; high throughput screening methods using magnetic resonance imaging agents)

REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:843946 CAPLUS

DOCUMENT NUMBER: 138:112124

Russel 09/674,526

TITLE: Characteristics of change in molecular weight of
DE-310 which is a polymeric drug with storage time
AUTHOR(S): Takeuchi, Masahito; Asai, Masahide; Tomitsuka,
Toshiaki; Sakai, Hideki; Abe, Masahiko
CORPORATE SOURCE: Tokyo Pharm. Res. Cent., Daiichi Pharm. Co., Ltd.,
Tokyo, 134-8630, Japan
SOURCE: Material Technology (Tokyo, Japan) (2002), 20(5),
242-247
CODEN: MTECFQ
PUBLISHER: Zairyo Gijutsu Kenkyu Kyokai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Carboxymethyldextran polyalc. camptothecin conjugate, which is a novel
polymeric drug, was synthesized, and is being developed as a code of
DE-310. We studied on the effects of storage temperature, excipients, and
water

content on the change in weight-average mol. weight, Mw, of lyophilized samples
containing DE-310. Mw of DE-310 in lyophilized samples with excipients
increased with storage time, and relationship between the rate of the
increment in Mw and storage temperature was able to be expressed as Arrhenius
plot. In addition, the sample having high glass transition temperature, Tg,
showed

low degree of the increment in Mw. The lyophilized samples with
disaccharides were higher Tg than one of samples with monosaccharides or
sugar alcs. The lyophilized sample with maltose showed the highest Tg in
the samples studied, and it was found that maltose especially suppressed
increasing in Mw with storage time.

CC 63-5 (Pharmaceuticals)

IT 9044-05-7D, Carboxymethyldextran, polyalc. conjugate with
camptothecin

RL: BCP (Biochemical process); PRP (Properties); BIOL (Biological study);
PROC (Process)

(characteristics of change in mol. weight of DE-310 during storage)

IT 200427-88-9

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(spacer; characteristics of change in mol. weight of DE-310 during
storage)

L4 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:148739 CAPLUS

DOCUMENT NUMBER: 136:205403

TITLE: DDS compounds of drugs having hydroxy groups

INVENTOR(S): Ousu, Satoru; Oki, Hitoshi; Naito, Hiroyuki; Hirotsu,
Kenji

PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002060351	A2	20020226	JP 2001-80188	20010321
PRIORITY APPLN. INFO.:			JP 2000-79655	A 20000322

OTHER SOURCE(S): MARPAT 136:205403

AB The DDS (drug delivery system) compds. are represented by the formula
AWN(R1)C(R2)(R3)OQ or PZN(R1)C(R2)(R3)OQ [A = polymeric carrier for drugs;

W = spacer containing amino acid or oligopeptide residue linked to N at the C-terminal; P = protective group for H or NH₂; Z = amino acid residue or oligopeptide residue linked to N at the C-terminal; R1-R3 = H, (substituted) alkyl, (substituted) aryl, carboxyl, alkoxy-carbonyl; 2 of R1-R3 may form 4- to 8-membered ring; OQ = residue of OH-containing drugs]. Tert-Bu 13-[[1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyloxy]-7-benzyl-2,5,8,11-tetraoxo-3,6,9,12-tetraazatri-1-decylcarbamate (preparation given) showed 89% release of 1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinol (I) in murine fibrosarcoma Meth-A cell homogenate at 40° and pH 4.5 and <1% release of I in a buffer at pH 4.5. I.v. administration of a carboxymethyl dextran polyol derivative of I (linked through an oligopeptide and aminomethylene linker) at 10 mg/kg as I showed significant antitumor effect and did not cause diarrhea in mice.

ICM A61K047-48
ICS A61K031-506; A61K047-36; A61K047-42; A61P029-00; A61P035-00; C07K005-103
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 33, 34
ST DDS peptide polysaccharide **carrier** antitumor drug; dextran **carrier** peptide spacer antitumor DDS
IT Polysaccharides, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **carriers**; preparation of amino acid or peptide derivs. of hydroxy-containing drugs for DDS)
IT 39422-83-8DP, Carboxymethyl dextran sodium salt, polyols, **conjugates** with peptide spacers and antitumor drugs
401470-32-4P 401470-34-6DP, **conjugates** with carboxymethyl dextran polyols 401470-36-8DP, **conjugates** with carboxymethyl dextran polyols 401470-38-0DP, **conjugates** with carboxymethyl dextran polyols 401470-40-4DP, **conjugates** with carboxymethyl dextran polyols 401470-44-8DP, **conjugates** with carboxymethyl dextran polyols 401470-48-2DP, **conjugates** with carboxymethyl dextran polyols 401470-52-8DP, **conjugates** with carboxymethyl dextran polyols 401470-56-2DP, **conjugates**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid or peptide derivs. of hydroxy-containing drugs for DDS)
IT 60667-52-9P 401470-30-2P 401470-31-3P 401470-33-5P 401470-34-6P
401470-35-7P 401470-36-8P 401470-37-9P 401470-38-0P
401470-39-1P 401470-40-4P 401470-41-5P 401470-42-6P 401470-43-7P
401470-44-8P 401470-45-9P 401470-46-0P 401470-47-1P 401470-48-2P
401470-49-3P 401470-50-6P 401470-51-7P 401470-52-8P 401470-53-9P
401470-54-0P 401470-55-1P 401470-56-2P 401470-58-4P 401470-60-8P
401470-61-9P 401470-62-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid or peptide derivs. of hydroxy-containing drugs for DDS)

ANSWER 7 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:77429 CAPLUS
DOCUMENT NUMBER: 136:139833
TITLE: Drug **conjugates** containing dicarboxy C1-3

Russel 09/674,526

INVENTOR(S): alkyldextran polyalcohols
Inoue, Kazuhiro; Suzuki, Hiroshi
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	JP 2002030002	A2	20020129	JP 2000-215919	20000717
PRIORITY APPLN. INFO.:				JP 2000-215919	20000717
AB	The invention relates to a drug conjugate wherein a dicarboxy C1-3 alkyldextran polyalc. is bonded to the residue of a medicinal compound, e.g. an antitumor agent and an antiinflammatory agent, with/without of a spacer consisting of one amino acid or a spacer consisting of 2-8 amino acids bonded to each other via peptide bonds. The conjugate exhibits excellent drug targeting property. Dextran polyalc. was reacted with diethylbromomalonate in the presence of cesium hydroxide to obtain dicarboxymethyl dextran polyalc. sodium salt. Cisplatin was reacted with AgNO3 and then, with the obtained dicarboxymethyl dextran polyalc. sodium salt. to make a conjugate. The conjugate showed sustained-release of low-mol.weight Pt compound in phosphate buffer.				
IC	ICM A61K047-48				
	ICS A61K031-282; A61K031-337; A61K031-4745; A61K031-505; A61K033-24; A61K045-00; A61P029-00; A61P035-00; C08B037-02				
CC	63-6 (Pharmaceuticals)				
ST	dicarboxyalkyl dextran polyalc drug conjugate prepn targeting				
IT	Anthracyclines				
	Taxanes				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor agents; drug conjugates containing dicarboxy C1-3 alkyldextran polyalcs.)				
IT	Carboxylic acids, reactions				
	RL: RCT (Reactant); RACT (Reactant or reagent) (dicarboxylic, C1--3 alkyl, halogenated; preparation of drug conjugates containing dicarboxy C1-3 alkyldextran polyalcs.)				
IT	Anti-inflammatory agents				
	Antitumor agents				
	Drug delivery systems (drug conjugates containing dicarboxy C1-3 alkyldextran polyalcs.)				
IT	Amino acids, biological studies				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (drug conjugates containing dicarboxy C1-3 alkyldextran polyalcs. and amino acid spacers)				
IT	Peptides, biological studies				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (drug conjugates containing dicarboxy C1-3 alkyldextran polyalcs. and peptide spacers)				
IT	Alkaloids, biological studies				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vinca, antitumor agents; drug conjugates containing dicarboxy C1-3 alkyldextran polyalcs.)				
IT	59-30-3; Folic acid, biological studies				
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; drug conjugates containing dicarboxy C1-3 alkyldextran polyalcs.)				

- IT 289-95-2D, Pyrimidine, fluoro derivs., **conjugates** with dicarboxyalkyl dextran polyalcs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agents; drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs.)
- IT 9004-54-0DP, Dextran, polyalcs., dicarboxymethyl derivs., **conjugates** with antitumor agents or antiinflammatory agents with/without of peptide spacers, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs.)
- IT 7689-03-4D, Camptothecin, derivs., **conjugates** with dicarboxyalkyl dextran polyalcs. 41575-94-4D, Carboplatin, **conjugates** with dicarboxyalkyl dextran polyalcs. 61825-94-3D, Oxaliplatin, **conjugates** with dicarboxyalkyl dextran polyalcs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs.)
- IT 685-87-0, Diethylbromomalonate 9004-54-0, Dextran T500, reactions 15663-27-1, Cisplatin 84275-35-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs.)
- IT 41575-87-5P 60732-70-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs.)
- IT 21351-79-1, Cesium hydroxide
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs.)
- IT 41575-87-5DP, **conjugates** with dicarboxymethyl dextran polyalcs. 60732-70-9DP, **conjugates** with dicarboxymethyl dextran polyalcs.
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs.)
- IT 200427-88-9DP, **conjugates** with dicarboxymethyl dextran polyalcs. and antitumor or antiinflammatory drugs
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of drug **conjugates** containing dicarboxy C1-3 alkyl dextran polyalcs. and peptide spacers)

L4 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:71911 CAPLUS
DOCUMENT NUMBER: 136:123681
TITLE: Pharmaceutical compositions containing DDS compounds
INVENTOR(S): Takahashi, Masayuki; Sugie, Shuichi; Takeuchi, Masahito
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005855	A1	20020124	WO 2001-JP6020	20010711
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001071037	A5	20020130	AU 2001-71037	20010711
EP 1308171	A1	20030507	EP 2001-949945	20010711
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012417	A	20030701	BR 2001-12417	20010711
NO 2003000139	A	20030313	NO 2003-139	20030110
US 2003148931	A1	20030807	US 2003-332706	20030113
PRIORITY APPLN. INFO.:			JP 2000-213083	A 20000713
			WO 2001-JP6020	W 20010711
AB	Disclosed are pharmaceutical compns. which contain compds. obtained by bonding a carboxyl-bearing polysaccharide derivative to a camptothecin derivative either through a spacer or not there through and are improved in storage stability by the addition of a sugar or a sugar alc. and, if necessary, a pH regulator. (1S,9S)-1-amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4- methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline- 10,13(9H,15H)-dione conjugates with carboxymethyldextran using Gly-Gly-Phe-Gly spacer, are formulated with maltose and pH modifier to pH 6-9 to have a freeze-dried composition			
IC	ICM A61K047-48 ICS A61K047-36; A61K047-26; A61K047-10; A61K009-19; A61K031-4745; C07D491-22			
CC	63-6 (Pharmaceuticals)			
ST	camptothecin dextran conjugate freeze dried compn			
IT	Antitumor agents			
	(antitumor compns. containing camptothecin derivative conjugates)			
IT	Polysaccharides, biological studies			
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor compns. containing camptothecin derivative conjugates)			
IT	Drug delivery systems			
	(freeze-dried; antitumor compns. containing camptothecin derivative conjugates)			
IT	Alcohols, biological studies			
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polyhydric; antitumor compns. containing camptothecin derivative conjugates)			
IT	50-69-1, Ribose 50-99-7, Glucose, biological studies 57-50-1, Saccharose, biological studies 58-86-6, Xylose, biological studies 59-23-4, Galactose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 69-79-4, Maltose 87-89-8, Inositol 99-20-7, Trehalose 512-69-6, Raffinose 528-50-7, Cellobiose 1109-28-0, Maltotriose 3458-28-4, Mannose 9044-05-7D, Carboxymethyldextran, camptothecin derivative conjugates 171335-80-1D, conjugates with peptide and carboxymethyldextran 200427-88-9D, conjugates with camptothecin derivative and carboxymethyldextran RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor compns. containing camptothecin derivative conjugates)			
REFERENCE COUNT:		10	THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS	

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2002:10548 CAPLUS
 DOCUMENT NUMBER: 136:74660
 TITLE: DDS compounds containing drug-carboxymethyl-dextran
 polyalcohol **conjugates** and process for
 preparation thereof
 INVENTOR(S): Imura, Akihiro; Noguchi, Shigeru; Yamaguchi, Tatsuya;
 Yagi, Tsutomu; Kawabe, Takefumi
 PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000734	A1	20020103	WO 2001-JP5498	20010627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001067831	A5	20020108	AU 2001-67831	20010627
EP 1298145	A1	20030402	EP 2001-945629	20010627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012287	A	20030506	BR 2001-12287	20010627
NO 2002006212	A	20030206	NO 2002-6212	20021223
US 2003166513	A1	20030904	US 2003-297584	20030502
PRIORITY APPLN. INFO.:			JP 2000-195919	A 20000629
			WO 2001-JP5498	W 20010627
AB	<p>Disclosed is a DDS compound which comprises (1S,9S)-1-amino-9-Et -5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]- pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13(9H,15H)-dione (I) as the drug compound and carboxymethyl-dextran polyalc. and in which the 1-position amino group of the former is bonded to the carboxyl groups of the latter through a spacer consisting of either one amino acid or 2 to 8 amino acids bonded by peptide linkages, characterized in that the amount of the drug compound residue introduced is 3.2-8.4 % and that the carboxymethyl-dextran polyalc. has an average mol. weight of 240,000-480,000 and a degree of carboxymethylation of 0.14-0.47. Also disclosed is a process for the preparation of the DDS compound which comprises the step of adding an aqueous solution of sodium periodate to an aqueous solution of dextran at a temperature of 4° ± 2° to oxidize the dextran, and then adding the resulting reaction fluid to an aqueous solution of sodium borohydride at a temperature of ≤ 15° to thereby obtain dextran polyalc. A conjugate of I and carboxymethyl-dextran polyalc. with tetrapeptide spacer Gly-Gly-Phe-Gly was prepared, and its antitumor effect in Meth A cell-bearing mice was examined</p>			
IC	ICM C08B037-02			
	ICS C07D491-22; A61K047-48; A61K031-4745; A61K047-36; A61P035-00			

Russel 09/674,526

- CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
- ST antitumor carboxymethyl-dextran polyalco **conjugate** peptide prepn
- IT Antitumor agents
Drug delivery systems
Drug delivery systems
(preparation of antitumor drug-carboxymethyl-dextran polyalco.
conjugates with peptide spacers)
- IT 1892-57-5, 1-Ethyl-3-(dimethylaminopropyl)carbodiimide 25952-53-8
RL: RGT (Reagent); RACT (Reactant or reagent)
(condensation agents; preparation of antitumor drug-carboxymethyl-dextran
polyalco. **conjugates** with peptide spacers)
- IT 9044-05-7DP, Carboxymethyl-dextran, polyalcs., Na salts, **conjugates**
with antitumor drug with peptide spacers 171335-80-1DP,
conjugates with peptide spacers and carboxymethyl-dextran polyalcs.
384828-78-8DP, reaction products with carboxymethyl-dextran
polyalco.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of antitumor drug-carboxymethyl-dextran polyalco.
conjugates with peptide spacers)
- IT 3926-62-3, Sodium monochloroacetate 9004-54-0, Dextran T-500, reactions
169869-90-3 **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antitumor drug-carboxymethyl-dextran polyalco.
conjugates with peptide spacers)
- IT 9004-54-0DP, Dextran, polyalcs. 9044-05-7DP, Carboxymethyl-dextran,
polyalcs., Na salts **223537-08-4P 384828-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of antitumor drug-carboxymethyl-dextran polyalco.
conjugates with peptide spacers)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:322648 CAPLUS

DOCUMENT NUMBER: 135:185307

TITLE: Characteristics of tissue distribution of various
polysaccharides as drug **carriers**: influences
of molecular weight and anionic charge on tumor
targeting

AUTHOR(S): Sugahara, Shuichi; Okuno, Satoshi; Yano, Toshiro;
Hamana, Hiroshi; Inoue, Kazuhiro

CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022,
Japan

SOURCE: Biological & Pharmaceutical Bulletin (2001), 24(5),
535-543

CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Using the Walker 256 model for carcinosarcoma-bearing rats, we i.v.
administered 5 polysaccharide carriers with various mol. wts. (MWs) and
elec. charges and tested for their plasma and tissue distribution. Two
carriers, carboxymethylated-D-manno-D-glucan (CMMG) and CMdextran (CMDex),
showed higher plasma AUC than the other carriers tested, namely, CMchitin
(CMCh), N-desulfated N-acetylated heparin (DSH), and hyaluronic acid (HA).
This was consistently found to be true over the range of MWs tested. For

CMDex, the maximum value of plasma AUC was obtained when the MW exceeded 150 kDa. As for the anionic charge, CMDex (110-180 kDa) with a degree of substitution (DS) of the CM groups ranging from 0.2 to 0.6, showed maximum plasma AUC values. Twenty-four hours after administration, the concentration

of

CMDex (180-250 kDa; DS: 0.6-1.2) in tumors was more than 3% of dose/g-approx. 10-fold higher than those observed with CMCh, DSH and HA. Doxorubicin (DXR) was bound to these carriers via a peptide spacer, GlyGlyPheGly (GGFG), to give carrier-GGFG-DXR conjugates (DXR content: 4.2-7.0 (weight/weight)%), and the antitumor effects of these conjugates were tested with Walker 256 carcinosarcoma-bearing rats by monitoring the tumor wts. after a single i.v. injection. Compared with free DXR, CMDex-GGFG-DXR and CMMG-GGFG-DXR conjugates significantly suppressed tumor growth, while the CMCh-GGFG-DXR, DSH-GGFG-DXR, and HA-GGFG-DXR conjugates in a similar comparison showed weak tumor growth inhibition. These findings suggest that the antitumor effect of the carrier-DXR conjugates was related to the extent with which the carriers accumulated in the tumors.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 33

ST doxorubicin polysaccharide **carrier** tumor targeting; antitumor

doxorubicin **conjugate** polysaccharide charge mol wt

IT Polysaccharides, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(acidic, **conjugates** with doxorubicin and peptide; effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT Drug delivery systems

(**carriers**; effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT Polysaccharides, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(**conjugates**, with doxorubicin and peptide; effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT Polysaccharides, biological studies

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(effects of mol. weight and anionic charge of polysaccharide **carriers** on doxorubicin tissue distribution and tumor targeting)

IT Antitumor agents

Drug targeting

Molecular weight

(effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT 9067-32-7DP, Hyaluronic acid sodium salt, **conjugates** with

doxorubicin and peptide 23214-92-8DP, Doxorubicin, **conjugates**

with peptide and polysaccharides 39422-83-8DP, Carboxymethyl dextran sodium salt, **conjugates** with doxorubicin and peptide

65667-26-7DP, **conjugates** with doxorubicin and peptide

105156-94-3DP, Carboxymethyl chitin sodium salt, **conjugates** with

doxorubicin and peptide 200427-88-9DP, **conjugates** with

doxorubicin and polysaccharides 355129-33-8DP, **conjugates** with doxorubicin and peptide
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

IT 9067-32-7P, Hyaluronic acid sodium salt 39422-83-8P, Carboxymethyl dextran sodium salt 65667-26-7P 105156-94-3P, Carboxymethyl chitin sodium salt 355129-33-8P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(effects of mol. weight and anionic charge of polysaccharide drug **carriers** on tumor targeting)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4. ANSWER 11 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN.

ACCESSION NUMBER: 2001:78410 CAPLUS

DOCUMENT NUMBER: 134:147856

TITLE: Preparation of polypeptide dendrimers as unimolecular **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs

INVENTOR(S): Verdini, Antonio

PATENT ASSIGNEE(S): Italy

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007469	A2	20010201	WO 2000-EP7022	20000721
WO 2001007469	A3	20010510		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1200461	A2	20020502	EP 2000-949393	20000721
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
JP 2003506326	T2	20030218	JP 2001-512552	20000721
NZ 517231	A	20030530	NZ 2000-517231	20000721
NO 2002000333	A	20020122	NO 2002-333	20020122
PRIORITY APPLN. INFO.:			IT 1999-FO15	A 19990723
			WO 2000-EP7022	W 20000721

AB The invention describes new polypeptide dendrimers and processes for their synthesis. The polypeptide dendrimers of the invention have a structure which consists of a multifunctional core moiety from which highly branched polypeptide chains, formed by short peptide branching units, extend radially outwards. The outermost branches surround a lower d. space with

hollows and channels into which bioactive substances employed in diagnosis and therapy can be entrapped or covalently linked. The said polypeptide dendrimers are particularly useful in a number of areas in biol. and medicine as carriers for the delivery of bioactive substances, including drugs, or as carriers of bacterial, viral and parasite antigens, gene-therapy compds. and diagnostic imaging contrast agents. $N[CH_2CH_2NHCOCH(CH_2Ph)NH-Gly-Gly-Orn-Gly[Gly-Gly-Orn(Boc)-Gly-Boc]_2]_3$ (Boc = tert-butoxycarbonyl) is an example of a polypeptide dendrimer which was synthesized. Various properties of the polypeptide dendrimers were studied, including stability to enzymic hydrolysis in vitro and immunogenicity in mice and its adjuvant activity when some of the NH_2 groups are covalently linked to the octapeptide antigen Ala-Asn-Pro-Asn-Ala-Asn-Pro-Asn.

- IC ICM C07K014-00
- CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 15, 63
- ST peptide dendrimer prepn **carrier** drug imaging contrast agent;
immunogen peptide dendrimer prepn
- IT Imaging agents
(contrast; preparation of polypeptide dendrimers as unimol. **carriers**
of diagnostic imaging contrast agents, bioactive substances and drugs)
- IT Dendritic polymers
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidyl; preparation of polypeptide dendrimers as unimol. **carriers**
of diagnostic imaging contrast agents, bioactive substances and drugs)
- IT Antibacterial agents
Antibiotics
Antitumor agents
Antiviral agents
Drug delivery systems
Gene therapy
(preparation of polypeptide dendrimers as unimol. **carriers** of
diagnostic imaging contrast agents, bioactive substances and drugs)
- IT Antigens
Peptides, preparation
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polypeptide dendrimers as unimol. **carriers** of
diagnostic imaging contrast agents, bioactive substances and drugs)
- IT 322475-89-8DP, acetylated 322475-92-3DP, acetylated 322475-92-3P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
(dendritic; preparation of polypeptide dendrimers as unimol.
carriers of diagnostic imaging contrast agents, bioactive
substances and drugs)
- IT 322475-89-8P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(dendritic; preparation of polypeptide dendrimers as unimol.
carriers of diagnostic imaging contrast agents, bioactive
substances and drugs)
- IT 322641-30-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(initiator core for dendritic polypeptide; preparation of polypeptide
dendrimers as unimol. **carriers** of diagnostic imaging contrast
agents, bioactive substances and drugs)
- IT 107-15-3P, 1,2-Ethanediamine, preparation 322641-29-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

- BIOL (Biological study); PREP (Preparation); USES (Uses)
(initiator core for dendritic polypeptides; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)
- IT 322475-87-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(initiator core for dendritic polypeptides; preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)
- IT 323178-52-5P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)
- IT 105869-23-6DP, **conjugates** with polypeptide dendrimers
323178-48-9P 323178-51-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)
- IT 556-50-3, Glycylglycine 2776-60-5, Glycylglycine methyl ester hydrochloride 4097-89-6, Tris(2-aminoethyl)amine 13734-34-4
139112-38-2, Tris(2-maleimidoethyl)amine 162827-98-7 322475-84-3
322475-90-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)
- IT 322475-75-2P 322475-76-3P 322475-78-5P 322475-79-6P 322475-80-9P
322475-81-0P 322475-82-1P 322475-83-2P 322475-85-4P 322475-86-5P
322648-79-3P 322648-81-7P **323178-50-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polypeptide dendrimers as unimol. **carriers** of diagnostic imaging contrast agents, bioactive substances and drugs)

L4 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:832857 CAPLUS

DOCUMENT NUMBER: 134:256691

TITLE: Determinants for the drug release from T-0128, camptothecin analog-carboxymethyl dextran conjugate

AUTHOR(S): Harada, M.; Sakakibara, H.; Yano, T.; Suzuki, T.; Okuno, S.

CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd., Yodogawa-ku, Osaka, 532-8505, Japan

SOURCE: Journal of Controlled Release (2000), 69(3), 399-412
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To improve pharmacol. profiles of camptothecins (CPTs), a new macromol. prodrug, denoted T-0128, was synthesized. This prodrug comprises a novel CPT analog (T-2513: 7-ethyl-10-aminopropylxy-CPT) bound to carboxymethyl (CM) dextran through a Gly-Gly-Gly linker, with a mol. weight of 130 kDa. The present study was designed to elucidate the mechanisms that promote the release of linked T-2513. First, we compared the abilities of a rat liver homogenate, a cocktail of its lysosomal enzymes, and different types of pure enzymes, to liberate T-2513 from the conjugate. The releasing

rate in the homogenate was very slow, but was accelerated with the lysosomes. Lysosomal cysteine proteinases, such as cathepsin B, were responsible, coupled with the results of in vitro and in vivo inhibition studies using proteinase inhibitors. The pH optimum for the cathepsin B-mediated drug release was approx. 4. This corresponds to the pH in lysosomes, suggesting lysosomotropic release. Second, to assess the effect of the length and composition of the peptidyl linker, we synthesized the conjugates with a different linker and compared the drug-releasing rates. We found that the insertion of Phe into Gly-Gly-Gly allowed various kinds of enzymes to produce a rapid cleavage, and the Gly-chain lengthening enhanced the lysosome-mediated drug release. The released T-2513 levels in the liver and tumor of the tumor-bearing rats dosed with each conjugate increased with the length of Gly linker, suggesting a good in vitro to in vivo relationship. Comparative efficacy studies of the conjugates with a different linker demonstrated that T-0128 showed the maximum efficacy against MX-1 human mammary xenograft tumors. Thus the Gly-Gly-Gly linker exploits lysosomal cathepsin B to release T-2513 slowly and steadily, resulting in improved therapeutic efficacy.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 26, 33, 34

ST camptothecin prodrug release dextran peptide **conjugate**

IT Antitumor agents

Dissolution rate

(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT Drug delivery systems

(prodrugs; determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT 288247-87-0, T 2513

RL: PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT 187852-51-3P, Glycinamide, glycyglycylglycyl-N-[3-[[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, compound with dextran carboxymethyl ether sodium salt 187852-60-4P, Glycinamide, glycyglycyl-N-[3-[[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, compound with dextran carboxymethyl ether sodium salt 187852-63-7P, T 0128 187852-64-8P, Glycinamide, glycyglycylglycylglycylglycyl-N-[3-[[[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, compound with dextran carboxymethyl ether sodium salt 193097-95-9P 330808-09-8P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT 4530-20-5, tert-Butoxycarbonylglycine 28320-73-2, Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycyglycyl- 31972-52-8, tert-Butoxycarbonylglycyglycine 39422-83-8, Sodium carboxymethyl dextran 174308-47-5, Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycyglycylglycyl- 187794-49-6 330807-97-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran **conjugate**)

IT 192991-32-5P 192991-33-6P 330807-98-2P 330807-99-3P 330808-00-9P 330808-01-0P 330808-02-1P 330808-03-2P 330808-04-3P 330808-05-4P 330808-06-5P 330808-07-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(determinants for drug release from T-0128 camptothecin
analog-carboxymethyl dextran **conjugate**)

IT 7689-03-4, Camptothecin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(determinants for drug release from T-0128 camptothecin
analog-carboxymethyl dextran **conjugate**)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:314580 CAPLUS

DOCUMENT NUMBER: 132:326152

TITLE: DDS compounds and method for assaying the same

INVENTOR(S): Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi;
Ikeda, Masahiro; Shiose, Yoshinobu; Korenaga, Hiroshi

PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025825	A1	20000511	WO 1999-JP6016	19991029
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9964880	A1	20000522	AU 1999-64880	19991029
AU 765409	B2	20030918		
BR 9915198	A	20010814	BR 1999-15198	19991029
EP 1155702	A1	20011121	EP 1999-952805	19991029
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
NO 2001002128	A	20010620	NO 2001-2128	20010430
ZA 2001004214	A	20020114	ZA 2001-4214	20010523

PRIORITY APPLN. INFO.:

JP 1998-310130 A 19981030
JP 1998-329272 A 19981119
WO 1999-JP6016 W 19991029

AB The invention relates to a method for assaying a DDS compound containing a saccharide compound-modified carboxy C1-4 alkyl dextran polyalc. and a drug compound [DX8951 or doxorubicin] residue bonded to this carboxy C1-4 alkyl dextran polyalc., or a DDS compound wherein a polymer carrier is bonded to a drug compound residue via a spacer containing 2 to 8 amino acids bonded together via peptide bonds, which involves the step of assaying a hydrolyzate obtained by treating the DDS compound with peptidase.

IC ICM A61K047-48

ICS A61K047-30; A61K047-26; A61K031-47

CC 64-3 (Pharmaceutical Analysis)

Section cross-reference(s): 1, 63

IT 23214-92-8DP, Doxorubicin, **conjugates** with carboxy C1-4
alkyl dextran polyalc. **carriers** 171335-80-1DP, DX 8951,

conjugates with carboxy C1-4 alkyl dextran polyalc.
carriers

RL: ANT (Analyte); SPN (Synthetic preparation); THU (Therapeutic use);
ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(DDS compds. and method for assaying the same)

IT 9044-05-7DP, Carboxymethyl dextran, polyalkyl and galactose- or
N-acetylgalactosamine-modified, DX8951 or doxorubicin **conjugates**
with **75853-32-6DP**, DX8951 or doxorubicin **conjugates**
with carboxy C1-4 alkyl dextran polyalc. and **200427-88-9DP**,
DX8951 or doxorubicin **conjugates** with carboxy C1-4 alkyl dextran
polyalc. and 267227-43-ODP, DX8951 or doxorubicin **conjugates**
with carboxy C1-4 alkyl dextran polyalc. and
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)

(DDS compds. and method for assaying the same)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:311210 CAPLUS

DOCUMENT NUMBER: 133:155250

TITLE: Distribution characteristics of carboxymethyl
pullulan-peptide-doxorubicin **conjugates** in
tumor-bearing rats: different sequence of peptide
spacers and doxorubicin contents

AUTHOR(S): Nogusa, Hideo; Yamamoto, Keiji; Yano, Toshiro; Kajiki,
Masahiro; Hamana, Hiroshi; Okuno, Satoshi

CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022,
Japan

SOURCE: Biological & Pharmaceutical Bulletin (2000), 23(5),
621-626

CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Plasma and tissue distribution of conjugates of CM-pullulan (CMPul) and
doxorubicin (DXR), either bound directly or through three types of
tetrapeptide spacers, was studied after i.v. injection to rats bearing
Walker 256 carcinosarcoma and compared with that of DXR. In contrast to
DXR, each conjugate retained high levels of DXR in the conjugated form in
plasma and displayed high accumulation in the tumor at 6 h after the
administration. Disposition characteristics of [3H]CMPul in rats bearing
Walker 256 carcinosarcoma indicate that pullulan, which had mol. weight over
50 kDa, is a suitable macromol. carrier for tumor targeting in cancer
chemotherapy by carboxymethylation. We find that the in vivo antitumor
effect of the conjugates depends on the tumor AUC of free DXR released
from the conjugates. CMPul-DXR conjugates were also distributed in the
reticuloendothelial organs, such as liver, spleen and bone marrow;
however, the tissue concns. of the conjugates in the heart, lung and
muscle were lower than those of DXR. We next investigated the effect of
the DXR contents of CMPul-DXR conjugates on their body distribution in
rats bearing Walker 256. The half life of CMPul-DXR conjugates in plasma
were shorter and the conjugates had greater accumulation in the
reticuloendothelial system, while they showed lower concns. in the tumor
with increasing DXR contents. Antitumor activity of CMPul-DXR conjugates
were reduced and the lethal toxicities of CMPul-DXR conjugates were
amplified with increasing DXR contents.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1

- ST doxorubicin pullulan peptide **conjugate** pharmacokinetics
antitumor
- IT Structure-activity relationship
(antitumor; peptide spacers and doxorubicin contents effect on
pharmacokinetics and antitumor activity of CM-pullulan-peptide-
doxorubicin **conjugates** in tumor-bearing rats)
- IT Drug delivery systems
(injections, i.v.; peptide spacers and doxorubicin contents effect on
pharmacokinetics and antitumor activity of CM-pullulan-peptide-
doxorubicin **conjugates** in tumor-bearing rats)
- IT Antitumor agents
(peptide spacers and doxorubicin contents effect on pharmacokinetics
and antitumor activity of CM-pullulan-peptide-doxorubicin
conjugates in tumor-bearing rats)
- IT 9057-02-7D, Pullulan, carboxymethyl derivs., reaction products with
doxorubicin 23214-92-8D, Doxorubicin, reaction products with sodium
carboxymethylpullulan **161254-06-4D**, reaction products with
sodium carboxymethylpullulan 161254-07-5D, reaction products with sodium
carboxymethylpullulan 161254-12-2D, reaction products with sodium
carboxymethylpullulan
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
effector, except adverse); BPR (Biological process); BSU (Biological
study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); PROC (Process); USES (Uses)
(peptide spacers and doxorubicin contents effect on pharmacokinetics
and antitumor activity of CM-pullulan-peptide-doxorubicin
conjugates in tumor-bearing rats)
- IT 23214-92-8, Doxorubicin
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM
(Metabolic formation); BIOL (Biological study); FORM (Formation,
nonpreparative); PROC (Process)
(peptide spacers and doxorubicin contents effect on pharmacokinetics
and antitumor activity of CM-pullulan-peptide-doxorubicin
conjugates in tumor-bearing rats)
- REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L4 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:146878 CAPLUS
DOCUMENT NUMBER: 132:288308
TITLE: Structure-activity relationships of
carboxymethylpullulan-peptide-doxorubicin
conjugates: Systematic modification of peptide
spacers
- AUTHOR(S): Nogusa, Hideo; Yano, Toshiro; Kashima, Nobukazu;
Yamamoto, Keiji; Okuno, Satoshi; Hamana, Hiroshi
- CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022,
Japan
- SOURCE: Bioorganic & Medicinal Chemistry Letters (2000),
10(3), 227-230
CODEN: BMCLE8; ISSN: 0960-894X
- PUBLISHER: Elsevier Science Ltd.
- DOCUMENT TYPE: Journal
- LANGUAGE: English
- AB A series of carboxymethylpullulan (CMPul)-doxorubicin (DXR) conjugates
bound by peptide spacers of different compns. and lengths were prepared and
evaluated for their in vivo antitumor effects. Systematic study of the
peptide spacers indicated that CMPul-DXR conjugates bound via appropriate
dipeptide spacers were more potent than DXR.
- CC 1-3 (Pharmacology)

Section cross-reference(s): 63
IT Structure-activity relationship
(antitumor; structure-antitumor activity relationships of
CM-pullulan-peptide-doxorubicin **conjugates**)
IT Drug delivery systems
(prodrugs; structure-antitumor activity relationships of
CM-pullulan-peptide-doxorubicin **conjugates**)
IT Antitumor agents
(structure-antitumor activity relationships of CM-pullulan-peptide-
doxorubicin **conjugates**)
IT 23214-92-8D, Doxorubicin, **conjugates** with CM-pullulan and
peptides 53571-87-2D, Carboxymethylpullulan, **conjugates** with
peptidyl doxorubicin 264192-71-4D, **conjugates** with CM-pullulan
264192-72-5D, **conjugates** with CM-pullulan
264192-73-6D, **conjugates** with CM-pullulan 264192-74-7D,
conjugates with CM-pullulan 264192-75-8D, **conjugates**
with CM-pullulan 264192-76-9D, **conjugates** with CM-pullulan
264192-77-0D, **conjugates** with CM-pullulan 264192-78-1D,
conjugates with CM-pullulan 264192-79-2D, **conjugates**
with CM-pullulan 264192-80-5D, **conjugates** with CM-pullulan
264192-81-6D, **conjugates** with CM-pullulan 264192-82-7D,
conjugates with CM-pullulan 264192-83-8D, **conjugates**
with CM-pullulan
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); PROC (Process); USES (Uses)
(structure-antitumor activity relationships of CM-pullulan-peptide-
doxorubicin **conjugates**)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:50615 CAPLUS

DOCUMENT NUMBER: 133:28087

TITLE: A triglycine **linker** improves tumor uptake
and biodistributions of 67-Cu-Labeled
anti-neuroblastoma MAb chCE7 F(ab')₂ fragments

AUTHOR(S): Zimmermann, K.; Gianollini, S.; Schubiger, P. A.;
Novak-Hofer, I.

CORPORATE SOURCE: Center for Radiopharmaceutical Sciences, Paul Scherrer
Institute, Villigen, Switz.

SOURCE: Nuclear Medicine and Biology (1999), 26(8), 943-950
CODEN: NMBIEO; ISSN: 0969-8051

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The peptide-linked copper chelators CPTA-triglycyl-L-p-isothiocyanato-
phenylalanine (CPTA-R1-NCS) as well as DOTA-triglycyl-L-p-isocyanato-
phenylalanine (DOTA-R1-NCS) were synthesized and coupled to F(ab')₂
fragments of the anti-neuroblastoma monoclonal antibody (MAb) chCE7.
67Cu-labeled conjugates were compared with the original CPTA- and
DO3A-F(ab')₂ in vitro and in vivo in mice bearing neuroblastoma
xenografts. With the CPTA-R1-F(ab')₂, biodistributions were improved,
because radioactivity present in the kidney was reduced. With the
DOTA-R1-F(ab')₂, clearance from the blood was slower and tumor uptake was
higher compared with the other conjugates. DOTA-R1-F(ab')₂ achieved the
best tumor/tissue ratios.

CC 8-9 (Radiation Biochemistry)

IT Drug delivery systems
(immunoconjugates, 67Cu-labeled; triglycine **linker** improves

tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')₂ fragments)

IT Antibodies

RL: RCT (Reactant); RACT (Reactant or reagent)

(monoclonal, chCE7, F(ab')₂ fragment; triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')₂ fragments)

IT Antibodies

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(monoclonal, labeled, 67Cu-labeled; triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')₂ fragments)

IT Nerve, neoplasm

(neuroblastoma; triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')₂ fragments)

IT Immunoradiotherapy

(triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')₂ fragments)

IT 273944-80-2DP, 67Cu-labeled MAb **conjugate**

273944-81-3DP, 67Cu-labeled MAb **conjugate**

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(triglycine **linker** improves tumor uptake and biodistributions of 67-Cu-Labeled anti-neuroblastoma MAb chCE7 F(ab')₂ fragments)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:763905 CAPLUS

DOCUMENT NUMBER: 132:15631

TITLE: Antitumor or antiinflammatory drug composites

INVENTOR(S): Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi

PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961061	A1	19991202	WO 1999-JP2681	19990521
W:				
AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,				
DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,				
JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,				
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,				
TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,				
RU, TJ, TM				
RW:				
GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2333321	AA	19991202	CA 1999-2333321	19990521
AU 9937333	A1	19991213	AU 1999-37333	19990521
EP 1080732	A1	20010307	EP 1999-919664	19990521
R:				
BE, CH, DE, FR, GB, IT, LI, NL, SE				
NO 2000005913	A	20010122	NO 2000-5913	20001122

PRIORITY APPLN. INFO.:

JP 1998-140915 A 19980522
WO 1999-JP2681 W 19990521

- AB Drug composites useful as DDS compds., which are represented by the general formula: A-R-NH-Y-CH₂-O-CO-Q (wherein A is a polymer serving as a carrier for a drug; R is a spacer comprising one amino acid mol. or one comprising 2 to 8 amino acid mols. bound to each other through peptide linkage; Y is optionally substituted phenylene; and Q is a residue of a drug compound such as an antitumor agent). The composites permit the speedy and regioselective release of drug compds. such as antitumor or anti-inflammatory agents, thus exhibiting expected drug effects without fail. A composite of DX-8951 [(1S,9S)-1-Amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-10,13(9H,15H)-dione] was prepared from DX-8951 methanesulfonic acid salt, dextran polyalc. Na salt, Boc-Gly-Gly-Phe-Gly-OH, 4-aminobenzylalc., and bis(4-nitrophenyl)carbonate.
- IC ICM A61K047-48
ICS A61K047-36; A61K009-00; A61K031-47; C07D491-22
- CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
- ST antitumor dextran polyalc peptide aminobenzylloxycarbonyl **conjugate**
; antiinflammatory dextran polyalc peptide aminobenzylloxycarbonyl **conjugate**
- IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aminobenzylloxycarbonyl, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs.; antitumor or antiinflammatory drug dextran polyalc. **conjugates**)
- IT Anti-inflammatory agents
Antitumor agents
Drug bioavailability
Drug delivery systems
Drug targeting
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)
- IT 64-19-7DP, Acetic acid, reaction products with dextran and Dx 8951 derivs., biological studies 9004-54-0DP, Dextran, polyalcs., **conjugates** with peptide-aminobenzylloxycarbonyl spacers and antitumor or antiinflammatory drugs, biological studies 9044-05-7DP, Carboxymethyldextran, polyalcs., **conjugates** with peptide-aminobenzylloxycarbonyl spacers and antitumor or antiinflammatory drugs 171335-80-1DP, DX 8951, reaction products with dextran-peptide-aminobenzylloxycarbonyl **conjugates** 251459-40-2DP, reaction products with dextran and acetic acid 251459-41-3DP, reaction products with dextran and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)
- IT 251459-33-3DP, reaction products with dextran and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor or antiinflammatory drug dextran polyalc. **conjugates**)
- IT 623-04-1, 4-Aminobenzylalcohol 5070-13-3, Bis(4-nitrophenyl)carbonate 169869-90-3 187794-49-6 251459-34-4
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of antitumor or antiinflammatory drug dextran polyalc.
conjugates)

IT 9044-05-7DP, Carboxymethyldextran, polyalcs., Na salts 31972-52-8P
251459-28-6P 251459-29-7P 251459-31-1P
251459-32-2P 251459-35-5P 251459-36-6P 251459-37-7P
251459-38-8P 251459-39-9P 251459-40-2DP, reaction
products with dextran and acetic acid 251459-41-3P 251459-42-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of antitumor or antiinflammatory drug dextran polyalc.
conjugates)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:224542 CAPLUS

DOCUMENT NUMBER: 130:316621

TITLE: Drug **conjugates** comprising carboxyalkyl
pullulan polyalcohol **carriers** bonded with
pharmaceutically active agents through peptide spacers
INVENTOR(S): Inoue, Kazuhiro; Suzuki, Hiroshi; Ikeda, Masahiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan; Dds Kenkyusho K. K.
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11092405	A2	19990406	JP 1997-254780	19970919
PRIORITY APPLN. INFO.:			JP 1997-254780	19970919

AB The invention provides a drug conjugate suitable for an improved drug
delivery system of an antitumor agent or an anti-inflammatory agent,
wherein the conjugate contains a carboxy C1-4 alkyl pullulan polyalc.
carrier bonded with a pharmaceutically active agent residue through a
spacer consisting of an amino acid or a peptide with 2-8 amino acids. An
antitumor conjugate consisting of carboxymethyl pullulan
polyalc.-Gly-Gly-Phe-Gly- (DX-8951) was prepared The conjugate exhibited
higher antitumor effect with lower injection doses in Meth A-bearing mice
as compared with the effect of unconjugated DX-8951.

IC ICM A61K047-48
ICS C07K005-103

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 33

ST carboxyalkyl pullulan peptide spacer antitumor **conjugate**

IT Drug delivery systems
(**carriers**; drug **conjugates** comprising carboxyalkyl
pullulan polyalc. **carriers** bonded with drugs through peptide
spacers)

IT Anti-inflammatory agents
Antitumor agents
Drug delivery systems
Drug targeting
(drug **conjugates** comprising carboxyalkyl pullulan polyalc.
carriers bonded with drugs through peptide spacers)

IT Drug delivery systems
(injections; drug **conjugates** comprising carboxyalkyl pullulan
polyalc. **carriers** bonded with drugs through peptide spacers)

- IT 79-11-8DP, reaction products with pullulan derivative and peptide-benzopyranoindolizinoquinoline **conjugate** 9057-02-7DP, Pullulan, oxidized, reduced, reaction products with chloroacetate and peptide-benzopyranoindolizinoquinoline **conjugate** 169869-90-3DP, reaction products with pullulan polyalc.-peptide **conjugate** 171335-80-1DP, reaction products with pullulan polyalc.-peptide **conjugate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)
- IT 23214-92-8D, Doxorubicin, reaction products with pullulan polyalc.-peptide **conjugate**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)
- IT 79-11-8, reactions 9057-02-7, Pullulan **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)
- IT **223537-08-4P 223537-11-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of drug **conjugates** comprising carboxyalkyl pullulan polyalc. **carriers** bonded with drugs through peptide spacers)

L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:698781 CAPLUS
DOCUMENT NUMBER: 130:106984
TITLE: Comparison of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6, a novel immunoconjugate with catabolizable **linker**, to 2-iminothiolane-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 in breast cancer xenografts
AUTHOR(S): DeNardo, Gerald L.; Kroger, Linda A.; Meares, Claude F.; Richman, Carol M.; Salako, Qansy; Shen, Sui; Lamborn, Kathleen R.; Peterson, James J.; Miers, Laird A.; Zhong, Gao Ren; DeNardo, Sally J.
CORPORATE SOURCE: Department of Internal Medicine, School of Medicine, University of California Davis, Sacramento, CA, 95816, USA
SOURCE: Clinical Cancer Research (1998), 4(10), 2483-2490
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Radioimmunotherapy using 131I-ChL6 antibody has shown promise in patients with breast cancer. To enhance this potential, a novel ChL6 immunoconjugate that is catabolizable and tightly binds 90Y and 111In was developed. The immunoconjugate, 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6, consists of the macrocyclic chelator DOTA linked to ChL6 by a peptide that is preferentially catabolized in the liver. The pharmacokinetic and dosimetric properties of the radioimmunoconjugates (RICs) 111In- and 90Y-DOTA-peptide-ChL6 and 111In- and 90Y-2-iminothiolane (2-IT)-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 were compared in athymic

mice bearing HBT3477 human breast cancer xenografts. Each of the RICs was stable in vivo and concentrated well in the xenografts. Liver concentration, cumulative radioactivity (activity over time), and radiation dose of the DOTA-peptide-ChL6 RICs were one-third to one-half of those of the corresponding 2-IT-2-[p(bromoacetamido)benzyl]-DOTA-ChL6 RICs. Indium-111 RICs were imperfect tracers for corresponding 90Y RICs, although their pharmacokinetics and radiation dosimetries were similar. The results of this study were consistent with previously published in vitro data, which indicated that the peptide linker of DOTA-peptide-ChL6 was catabolized by cathepsin B. The cumulative activities and radiation doses to the liver of DOTA-peptide-ChL6 RICs were one-half of those of corresponding RICs with the 2-IT linker. Preliminary data from pilot studies in patients with breast cancer are in accord with these observations. These novel DOTA-peptide RICs seem to have excellent clin. potential for radioimmunotherapy associated with marrow transplantation, for which liver radiation is likely to be dose limiting for 90Y.

CC 8-9 (Radiation Biochemistry)

IT Antibodies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(conjugates; comparison of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6 radioimmunoconjugate to 2-iminothiolane-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 radioimmunoconjugate in breast cancer xenografts)

IT 6539-14-6D, 2-Iminothiolane, immunoconjugate with DOTA and ChL6 antibody 219721-93-4D, radioimmunoconjugate with DOTA and ChL6 antibody

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comparison of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA)-peptide-ChL6 to 2-iminothiolane-2-[p-(bromoacetamido)benzyl]-DOTA-ChL6 in breast cancer xenografts)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:665874 CAPLUS

DOCUMENT NUMBER: 130:4084

TITLE: Preparation of polysaccharide-peptide or amino acid-linked camptothecin conjugates as antitumor agents

INVENTOR(S): Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Akira; Yano, Toshiaki

PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

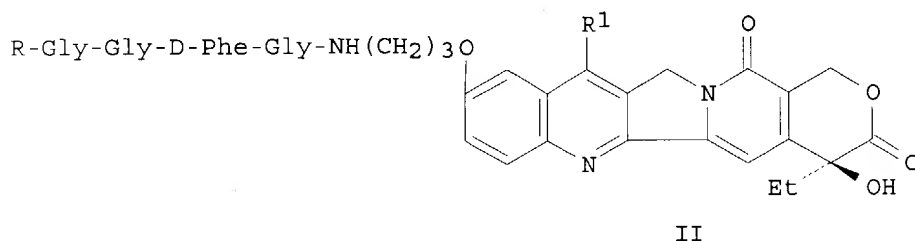
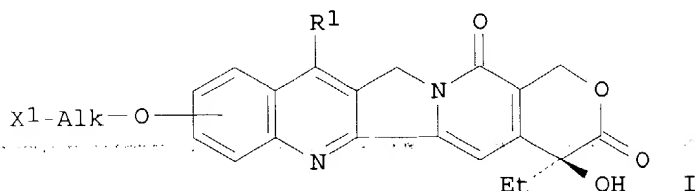
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10273488	A2	19981013	JP 1998-16763	19980129
JP 3322203	B2	20020909		

PRIORITY APPLN. INFO.: JP 1997-17280 A 19970131

OTHER SOURCE(S): MARPAT 130:4084

GI



- AB The title compds., which are camptothecin derives. [I; R1 = (un)substituted lower alkyl; X1 = NHR2, OH; wherein R2 = H, lower alkyl; Alk = linear or branched alkylene optionally interrupted by O] linked to carboxy-containing polysaccharide through a peptide or amino acid, are prepared. These compds. are reduced in toxicity and markedly enhanced in antitumor potency. Claimed is a pharmaceutical composition containing I as the active ingredient for treatment of cancers of lung, uterus, ovary, breast, digestive organs (large intestine, stomach, or pancreas), liver, kidney, prostate gland, and neck, malignant lymphoma, and leukemia. Thus, N-peptidyl-10-(3-aminopropoxy)-(20S)-camptothecin derivative (II; R = H) (preparation given) was condensed with carboxymethyl dextran sodium salt using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in H2O to give the title compound II (R = carboxymethyl dextran sodium salt residue), which at 60 mg/kg (single dosage) in vivo inhibited 100% the proliferation of human breast cancer MX-1 cell in mice within 26 days after the drug administration.
- IC ICM C07D491-22
ICS A61K031-47
- CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
- ST polysaccharide peptide **linked** camptothecin **conjugate** prepn; antitumor camptothecin **conjugate**; amino acid **linked** camptothecin polysaccharide prepn
- IT Antitumor agents
Antitumor agents
(digestive tract; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)
- IT Liver, neoplasm
(hepatoma, inhibitors; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)
- IT Antitumor agents
(hepatoma; preparation of polysaccharide-peptide or amino acid-**linked** camptothecin **conjugates** as antitumor agents)
- IT Kidney, neoplasm
Kidney, neoplasm

Lung, neoplasm
Pancreas, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
Uterus, neoplasm
Uterus, neoplasm
(inhibitors; preparation of polysaccharide-peptide or amino acid-
linked camptothecin conjugates as antitumor agents)

IT Antitumor agents
Antitumor agents
(kidney; preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(leukemia; preparation of polysaccharide-peptide or amino acid-
linked camptothecin conjugates as antitumor agents)

IT Antitumor agents
(lung; preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(mammary gland; preparation of polysaccharide-peptide or amino acid-
linked camptothecin conjugates as antitumor agents)

IT Antitumor agents
(neck; preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT Digestive tract
Digestive tract
Mammary gland
Neck, anatomical
Neck, anatomical
Prostate gland
(neoplasm, inhibitors; preparation of polysaccharide-peptide or amino acid-
linked camptothecin conjugates as antitumor agents)

IT Antitumor agents
Antitumor agents
(pancreas; preparation of polysaccharide-peptide or amino acid-
linked camptothecin conjugates as antitumor agents)

IT Antitumor agents
(preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT Amino acids, preparation
Glycoconjugates
Glycopeptides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
(prostate gland; preparation of polysaccharide-peptide or amino acid-
linked camptothecin conjugates as antitumor agents)

IT Antitumor agents
(stomach; preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT Antitumor agents
Antitumor agents
(uterus; preparation of polysaccharide-peptide or amino acid-**linked**
camptothecin **conjugates** as antitumor agents)

IT 39422-83-8DP, Carboxymethyl dextran sodium salt, **conjugates** with
peptide-**linked** camptothecin derivs. 53571-87-2DP,
Carboxymethyl pullulan, **conjugates** with peptide-**linked**

camptothecin derivs., sodium salt 187793-65-3P 187793-71-1P
 187794-13-4P 187794-21-4P 187794-24-7P 187794-27-0P 187794-30-5P
 187794-33-8P 187794-36-1P **187803-18-5DP**, bound to
 carboxymethyl dextran sodium salt 187803-20-9DP, bound to carboxymethyl
 dextran sodium salt 187803-20-9DP, bound to carboxymethyl pullulan
 sodium salt **187803-21-0DP**, bound to carboxymethyl dextran sodium
 salt **187803-22-1DP**, bound to carboxymethyl dextran sodium salt
 187803-23-2DP, bound to carboxymethyl dextran sodium salt
187803-26-5DP, bound to carboxymethyl dextran sodium salt
187803-27-6DP, bound to carboxymethyl dextran sodium salt
 187803-28-7DP, bound to carboxymethyl dextran sodium salt
187803-29-8DP, bound to carboxymethyl dextran sodium salt
187803-30-1DP, bound to carboxymethyl dextran sodium salt
 187803-31-2DP, bound to carboxymethyl dextran sodium salt 187803-32-3DP,
 bound to carboxymethyl dextran sodium salt **187803-33-4DP**, bound
 to carboxymethyl dextran sodium salt 187803-34-5DP, bound to
 carboxymethyl dextran sodium salt 187803-35-6DP, bound to carboxymethyl
 dextran sodium salt 215591-97-2DP, bound to carboxymethyl dextran sodium
 salt 215591-98-3DP, bound to carboxymethyl dextran sodium salt
 215592-03-3P 215592-06-6P 215592-09-9P 215592-15-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of polysaccharide-peptide or amino acid-linked
 camptothecin **conjugates** as antitumor agents)

IT 79-11-8, Chloroacetic acid, reactions 98-59-9, Tosyl chloride
 156-87-6, 3-Aminopropanol 627-30-5, 3-Chloropropanol 1826-67-1,
 Vinylmagnesium bromide 3978-80-1 9004-54-0, Dextran, reactions
 9057-02-7, Pullulan 15761-38-3 17302-47-5 18162-48-6,
 tert-Butyldimethylsilyl chloride 24424-99-5, Di-tert-butyl dicarbonate
 28782-81-2 42454-06-8, 5-Hydroxy-2-nitrobenzaldehyde 110351-94-5
 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of polysaccharide-peptide or amino acid-linked
 camptothecin **conjugates** as antitumor agents)

IT 39422-83-8P, Carboxymethyl dextran sodium salt 53571-87-2DP,
 Carboxymethyl pullulan, sodium salt 58885-58-8P 80909-96-2P
 187793-42-6P 187793-43-7P 187793-44-8P 187793-46-0P 187793-48-2P
 187793-52-8P 187793-56-2P 187793-58-4P 187793-60-8P 187793-62-0P
 187793-67-5P 187793-69-7P 187793-76-6P **187793-80-2P**
187793-82-4P 187793-84-6P 187793-86-8P
 187794-01-0P 187794-03-2P 187794-05-4P 187794-07-6P 187794-09-8P
 187794-11-2P 187794-17-8P 187794-19-0P 187794-20-3P 187794-22-5P
 187794-23-6P 187794-25-8P 187794-26-9P 187794-28-1P 187794-29-2P
 187794-31-6P 187794-32-7P 187794-34-9P 187794-35-0P 187794-47-4P
187794-50-9P 187794-55-4P 187794-58-7P
187794-60-1P 187794-66-7P 187794-68-9P 187794-70-3P
 187794-72-5P **187794-74-7P** 187803-36-7P 187803-37-8P
 205647-87-6P 215591-99-4P **215592-00-0P** 215592-01-1P
 215592-02-2P 215592-04-4P 215592-05-5P 215592-07-7P 215592-08-8P
 215592-10-2P 215592-11-3P 215592-12-4P **215592-13-5P**
215592-14-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of polysaccharide-peptide or amino acid-linked
 camptothecin **conjugates** as antitumor agents)

L4 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1998:1393 CAPLUS
 DOCUMENT NUMBER: 128:66510
 TITLE: Process for producing drug complexes

Russel 09/674,526

INVENTOR(S): Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan; Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND.	DATE	APPLICATION NO.	DATE
WO 9746261	A1	19971211	WO 1997-JP1915	19970605
W:		AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
TW 409058	B	20001021	TW 1997-86107456	19970531
AU 9729788	A1	19980105	AU 1997-29788	19970605
AU 723442	B2	20000824		
CN 1227500	A	19990901	CN 1997-197115	19970605
EP 955064	A1	19991110	EP 1997-924326	19970605
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI		
NO 9805667	A	19990204	NO 1998-5667	19981204
KR 2000016371	A	20000325	KR 1998-709945	19981204
US 6291671	B1	20010918	US 1999-147341	19990322
PRIORITY APPLN. INFO.:			JP 1996-144522 A	19960606
			WO 1997-JP1915 W	19970605

AB The invention relates to a process for producing drug complexes wherein a carboxylated polysaccharide derivative is bonded to a medicinal compound residue

via a spacer consisting of an amino acid or a spacer consisting of two to eight amino acids bonded to each other via peptide bonds, or drug complexes wherein a carboxylated polysaccharide derivative is bonded to a medicinal compound residue via no spacer, which is characterized by reacting in a nonaq. system an organic amine salt of the carboxylated polysaccharide derivative with the medicinal compound or the spacer bonded thereto. Thus, the reaction between the carboxylated polysaccharide derivative and the medicinal compound bonded to the spacer, etc., can be effected to achieve a high yield and side reactions can be inhibited in the case where, for example, the medicinal compound is one having a lactone ring.

IC ICM A61K047-48

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST anticancer antiinflammatory drug polysaccharide **conjugate**

IT Anti-inflammatory agents

Antitumor agents

Drug bioavailability

(anticancer and antiinflammatory drug-polysaccharide **conjugates**

)

IT Polysaccharides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**conjugates** with anticancer and antiinflammatory drugs and peptide spacers; anticancer and antiinflammatory drug-polysaccharide **conjugates**)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(conjugates with anticancer and antiinflammatory drugs and polysaccharides; anticancer and antiinflammatory drug-polysaccharide conjugates)

IT 56-40-6DP, Glycine, conjugates with antitumor and antiinflammatory drugs and polysaccharides, biological studies
637-84-3DP, conjugates with antitumor and antiinflammatory drugs and polysaccharides 721-90-4DP, conjugates with antitumor and antiinflammatory drugs and polysaccharides 9004-54-0DP, Dextran, oxidation and reduction derivs., conjugates with antitumor and antiinflammatory drugs and peptide spacers, biological studies
14656-09-8DP, conjugates with antitumor and antiinflammatory drugs and polysaccharides 23214-92-8DP, Doxorubicin, conjugates with peptide spacers and polysaccharides 66328-74-3DP, conjugates with antitumor and antiinflammatory drugs and polysaccharides 143655-66-7DP, conjugates with peptide spacers and polysaccharides 171335-80-1DP, conjugates with peptide spacers and polysaccharides 184585-36-2DP, conjugates with antitumor and antiinflammatory drugs and polysaccharides 200427-88-9DP, conjugates with antitumor and antiinflammatory drugs and polysaccharides 200427-89-0DP, conjugates with antitumor and antiinflammatory drugs and polysaccharides 200428-32-6DP, conjugates with peptide spacers and polysaccharides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(anticancer and antiinflammatory drug-polysaccharide conjugates)

L4 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:1392 CAPLUS

DOCUMENT NUMBER: 128:66509

TITLE: Drug complexes

INVENTOR(S): Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro; Kuga, Hiroshi; Kumazawa, Eiji; Togo, Akiko

PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan; Drug Delivery System Institute, Ltd.; Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro; Kuga, Hiroshi; Kumazawa, Eiji; Togo, Akiko

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746260	A1	19971211	WO 1997-JP1914	19970605
W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			

TW 527183	B	20030411	TW 1997-86107455	19970531
AU 9729787	A1	19980105	AU 1997-29787	19970605
AU 723392	B2	20000824		
EP 916348	A1	19990519	EP 1997-924325	19970605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1227499	A	19990901	CN 1997-197008	19970605
NO 9805666	A	19990204	NO 1998-5666	19981204
KR 2000016558	A	20000325	KR 1998-710148	19981207
US 6436912	B1	20020820	US 1999-147342	19990325
US 2003171262	A1	20030911	US 2002-155170	20020528
PRIORITY APPLN. INFO.:			JP 1996-144421	A 19960606
			WO 1997-JP1914	W 19970605
			US 1999-147342	A3 19990325

- AB The invention relates to drug complexes wherein a carboxy (C1-4)alkyldextran polyalc., which has been treated under such conditions as to allow the substantially complete formation of the polyalc., is bonded to the residue of a medicinal compound such as an antitumor agent [e.g. doxorubicin] via a spacer consisting of one amino acid or a spacer consisting of two to eight amino acids bonded to each other via peptide bonds. The complexes are excellent in the tumor site selectivity and thus can exhibit a high antitumor effect with relieved expression of toxicity.
- IC ICM A61K047-48
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 1
- ST antitumor drug dextran polyalc **conjugate**; antiinflammatory drug dextran polyalc **conjugate**; bioavailability drug dextran polyalc **conjugate**
- IT Anti-inflammatory agents
Antitumor agents
Drug bioavailability
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)
- IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs.; antitumor or antiinflammatory drug dextran polyalc. **conjugates**)
- IT 637-84-3D, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 23214-92-8D, Doxorubicin, **conjugates** with peptide spacer and carboxyalkyldextran polyalcs. 143655-66-7D, DW 8089, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs. 171335-80-1D, **conjugates** with peptide spacer and carboxyalkyldextran polyalcs. 184585-36-2D, D 51-7059, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs. 200427-88-9D, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 200438-24-0D, DW 8286, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)
- IT 56-40-6DP, Glycine, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs., preparation 721-90-4DP, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 9004-54-0DP, Dextran, oxidation and reduction

derivs., **conjugates** with peptide spacers and antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs., preparation 14656-09-8DP, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. 66328-74-3P 200427-89-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(antitumor or antiinflammatory drug dextran polyalc. **conjugates**)

L4 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:706907 CAPLUS

DOCUMENT NUMBER: 128:30115

TITLE: Antitumor effects and toxicities of carboxymethylpullulan-peptide-doxorubicin **conjugates**

AUTHOR(S): Nogusa, Hideo; Yano, Toshiro; Kajiki, Masahiro;

Gonsho, Akinori; Hamana, Hiroshi; Okuno, Satoshi

CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Noda, 278, Japan

SOURCE: Biological & Pharmaceutical Bulletin (1997), 20(10), 1061-1065

CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In vivo antitumor effects of the conjugates of doxorubicin (DXR) with carboxymethylpullulan (CMPul) through tetrapeptide spacers were compared with those of DXR against tumor-bearing rats. CMPul-DXR conjugates bound through Gly-Gly-Phe-Gly and Gly-Phe-Gly-Gly spacers were found to be more potent than DXR after a single i.v. injection in rats bearing Walker 256 carcinosarcoma. These conjugates were also more effective than DXR in rats bearing Yoshida sarcoma. However, CMPul-DXR conjugate bound through Gly-Gly-Gly-Gly was less effective against Walker 256-bearing rats than DXR. Body weight loss of CMPul-DXR conjugates in rats, on the other hand, was less than that of DXR at a DXR dose of 10 mg/kg. LDs of CMPul-DXR conjugates in CDF1 mice were about 3-times higher than that of DXR. These data suggest that the therapeutic index of CMPul-DXR conjugates bound through appropriate peptide spacers was increased more than that of DXR. However, CMPul-DXR conjugates tested were all less effective than DXR against Walker 256 cells in vitro. Also, 125I-labeled CMPul-DXR conjugate accumulated much less in the cells than 14C-DXR.

CC 1-6 (Pharmacology)

ST antitumor carboxymethylpullulan peptide doxorubicin **conjugate**

IT Antitumor agents
(antitumor effects and toxicities of carboxymethylpullulan-peptide-doxorubicin **conjugates**)

IT 161254-06-4 161254-07-5 161254-12-2

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antitumor effects and toxicities of carboxymethylpullulan-peptide-doxorubicin **conjugates**)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:211123 CAPLUS

DOCUMENT NUMBER: 126:199707

TITLE: Camptothecin derivatives

INVENTOR(S): Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Satoshi; Yano, Toshiro

Russel 09/674,526

PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 53 pp.

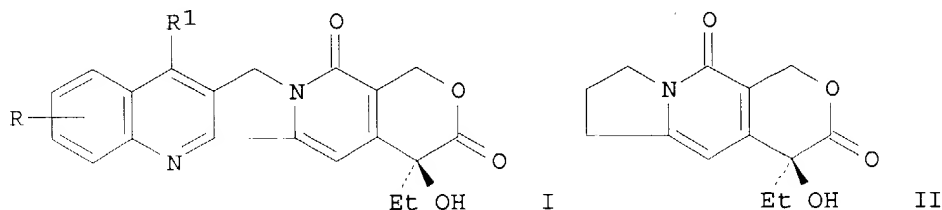
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 757049	A1	19970205	EP 1996-305579	19960730
EP 757049	B1	19990324		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AU 9660698	A1	19970206	AU 1996-60698	19960725
AU 717653	B2	20000330		
ZA 9606323	A	19970227	ZA 1996-6323	19960725
IL 118957	A1	20001121	IL 1996-118957	19960725
IL 127135	A1	20001206	IL 1996-127135	19960725
IL 131372	A1	20010319	IL 1996-131372	19960725
CA 2182244	AA	19970203	CA 1996-2182244	19960729
CA 2182244	C	20040203		
JP 10072467	A2	19980317	JP 1996-198939	19960729
JP 3332735	B2	20021007		
US 5837673	A	19981117	US 1996-689018	19960730
AT 178067	E	19990415	AT 1996-305579	19960730
ES 2131913	T3	19990801	ES 1996-305579	19960730
BG 63342	B1	20011031	BG 1996-100758	19960731
NO 9603214	A	19970203	NO 1996-3214	19960801
BR 9603253	A	19980428	BR 1996-3253	19960801
RU 2138503	C1	19990927	RU 1996-115394	19960801
CN 1145365	A	19970319	CN 1996-106979	19960802
CN 1075501	B	20011128		
TW 466242	B	20011201	TW 1996-85109331	19960802
HK 1005545	A1	20000414	HK 1998-104671	19980529
CN 1308078	A	20010815	CN 2000-132661	20001122
PRIORITY APPLN. INFO.:			JP 1995-197391	A 19950802
			JP 1995-340619	A 19951227
			JP 1996-173372	A 19960703
			IL 1996-118957	A3 19960725
			IL 1996-127135	A3 19960725
OTHER SOURCE(S):			MARPAT 126:199707	
GI				



AB Camptothecin derivs. I [R = aminoalkoxy, optionally bound to a polysaccharide having carboxyl groups via an amino acid or peptide; R1 = (un)substituted alkyl] were prepared I show enhanced antitumor activities but few side effects (no data). Thus, 10-(3-aminopropoxy)-7-ethyl-(20S)-

camptothecin.HCl was prepared from H₂N(CH₂)₃OH, 5,2-HO(O₂N)C₆H₃CHO, and the pyranoinidole II in 8 steps and was converted to its glycyl-glycyl-L-phenylalanyl-glycylaminopropoxy derivative which was treated with carboxymethyldextran Na salt to give the conjugate.

IC ICM C07D491-22

ICS A61K047-48; C08B037-00; C07K007-00; C07K005-00

CC 31-5 (Alkaloids)

Section cross-reference(s): 1

ST dextran **conjugate** peptidylaminoalkoxycamptothecin prepn
antitumor; camptothecin peptidylaminoalkoxy dextran **conjugate**
prepn antitumor

IT Antitumor agents

(preparation of dextran **conjugates** of
peptidylaminoalkoxy(ethyl)camptothecin)

IT 156-87-6, 3-Aminopropanol 3262-72-4, N-tert-Butoxycarbonyl-L-serine
3978-80-1, N-tert-Butoxycarbonyl-L-tyrosine 9004-54-0, Dextran,
reactions 9057-02-7, Pullulan 15761-38-3, N-tert-Butoxycarbonyl-L-
alanine 17302-47-5 25616-33-5 42454-06-8, 5-Hydroxy-2-
nitrobenzaldehyde 110351-94-5 174308-47-5 **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of dextran **conjugates** of
peptidylaminoalkoxy(ethyl)camptothecin)

IT 39422-83-8P, Carboxymethyldextran sodium salt 58885-58-8P 80909-96-2P
109116-58-7P, Pullulan, carboxymethyl ether, sodium salt 187793-42-6P
187793-43-7P 187793-44-8P 187793-45-9P 187793-46-0P 187793-48-2P
187793-50-6P 187793-52-8P 187793-54-0P 187793-56-2P 187793-62-0P
187793-67-5P 187793-69-7P 187793-74-4P 187793-76-6P
187793-78-8P 187793-80-2P 187793-84-6P
187793-86-8P 187793-88-0P 187793-90-4P 187794-01-0P
187794-03-2P 187794-05-4P 187794-07-6P 187794-11-2P 187794-17-8P
187794-19-0P 187794-20-3P 187794-22-5P 187794-23-6P 187794-25-8P
187794-26-9P 187794-28-1P 187794-29-2P 187794-31-6P 187794-32-7P
187794-34-9P 187794-35-0P 187794-37-2P 187794-38-3P 187794-40-7P
187794-41-8P 187794-43-0P 187794-44-1P 187794-46-3P 187794-47-4P
187794-48-5P 187794-50-9P 187794-53-2P
187794-55-4P 187794-60-1P 187794-66-7P 187794-68-9P
187794-72-5P **187794-74-7P** 187803-36-7P 187803-37-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of dextran **conjugates** of
peptidylaminoalkoxy(ethyl)camptothecin)

IT 187793-58-4P 187793-60-8P 187793-65-3P 187793-71-1P 187794-09-8P
187794-13-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of dextran **conjugates** of
peptidylaminoalkoxy(ethyl)camptothecin)

IT **187793-82-4P** 187794-21-4P 187794-24-7P 187794-27-0P
187794-30-5P 187794-33-8P 187794-36-1P 187794-39-4P 187794-42-9P
187794-45-2P 187794-58-7P 187794-70-3P **187852-47-7P**
187852-48-8P **187852-49-9P 187852-50-2P** 187852-51-3P
187852-52-4P 187852-53-5P 187852-54-6P **187852-55-7P**
187852-56-8P 187852-57-9P **187852-58-0P**
187852-59-1P 187852-60-4P 187852-61-5P **187852-62-6P**
187852-63-7P 187852-64-8P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)

(preparation of dextran **conjugates** of
peptidylaminoalkoxy(ethyl)camptothecin)

Russel 09/674,526

ACCESSION NUMBER: 1996:494751 CAPLUS
DOCUMENT NUMBER: 125:204516
TITLE: Diagnostic and therapeutic pretargeting methods using metal chelates
INVENTOR(S): Yau, Eric K.; Theodore, Louis J.; Gustavson, Linda M.
PATENT ASSIGNEE(S): Neorx Corporation, USA
SOURCE: U.S., 68 pp., Cont.-in-part of U.S. Ser. No. 156,565, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5541287	A	19960730	US 1994-345811	19941122
US 5283342	A	19940201	US 1992-895588	19920609
EP 1138334	A2	20011004	EP 2001-201994	19930607
EP 1138334	A3	20020403		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6022966	A	20000208	US 1993-156565	19931122
US 5911969	A	19990615	US 1994-329617	19941026
US 5847121	A	19981208	US 1995-571816	19951213

PRIORITY APPLN. INFO.:

US 1992-895588	A2	19920609
US 1992-995381	B2	19921223
US 1993-156565	B2	19931122
US 1992-995383	A	19921223
EP 1993-915235	A3	19930607
WO 1993-US5406	A2	19930607
US 1994-345811	A3	19941122

OTHER SOURCE(S): CASREACT 125:204516; MARPAT 125:204516

AB Methods, compds., compns., and kits that relate to pretargeted delivery of diagnostic (e.g. imaging) and therapeutic agents are disclosed. A targeting moiety-antiligand conjugate is administered in vivo; upon target localization of this conjugate (pretargeting) and clearance of the conjugate from the circulation, an active agent-ligand conjugate is parenterally administered. Alternatively, a targeting moiety-ligand conjugate is administered in vivo; upon target localization and clearance of the conjugate from the circulation, an active agent-antiligand conjugate is parenterally administered. A preferred ligand-antiligand pair is biotin and avidin. Preferred targeting moieties are antibodies, antibody fragments, peptides, hormones, oligonucleotides, and cell surface receptor proteins. Preferred active agents are toxins, antitumor agents, drugs, and radionuclides. In particular, methods for production of low-mol.-weight radioiodinated biotin derivs., and for radiometal labeling of biotin and related compds. with ^{99m}Tc, ¹⁸⁶Re, and ¹⁸⁸Re by conjugation with a metal-chelating moiety are described. Thus, p-aminobenzyl-1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (I) was prepared in several steps from N-tert-butoxycarbonylglycine p-nitrophenyl ester, ethylenediamine, and N-iodoacetyl-p-nitrophenylalanine using benzotriazolylxytris(dimethylamino)phosphonium hexafluorophosphate for cyclocondensation; I was then coupled with N-biotinyl-N-methylglycine and complexed with ⁹⁰Y. The chelate and its sulfoxide radiolysis product bound to avidin.

IC ICM A61K038-12
ICS C07K005-00

NCL 530317000

CC 63-6 (Pharmaceuticals)

ST antitumor pretargeting biotin conjugate avidin; radioelement

- biotin chelate targeting tumor; imaging radioelement chelate
conjugate targeting
- IT Neoplasm
(imaging of, with radioelement chelate-biotin **conjugates**;
diagnostic and therapeutic pretargeting methods using metal chelates)
- IT Neoplasm inhibitors
(radioelement chelate-biotin **conjugates**; diagnostic and
therapeutic pretargeting methods using metal chelates)
- IT Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biotinylated, galactosylated, antibody-streptavidin **conjugate**
clearance from blood in response to; diagnostic and therapeutic
pretargeting methods using metal chelates)
- IT Avidins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**, complexation with biotinylated antibody, for
pretargeting; diagnostic and therapeutic pretargeting methods using
metal chelates)
- IT Biological transport
(endocytosis, of radiolabeled biotin **conjugate**, pretargeting
in relation to; diagnostic and therapeutic pretargeting methods using
metal chelates)
- IT 58-85-5DP, D-Biotin, **conjugates** with radioactive metal chelates
9004-54-0DP, Dextran, biotinylated, radiolabeled 180737-57-9P
180737-58-0P 180737-59-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(diagnostic and therapeutic pretargeting methods using metal chelates)
- IT 25104-18-1D, Polylysine, **conjugates** with biotin and chelating
agents 38000-06-5D, Polylysine, **conjugates** with biotin and
chelating agents
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(diagnostic and therapeutic pretargeting methods using metal chelates)
- IT 1926-80-3P, Methyl 6-aminocaproate hydrochloride 3655-05-8P
14273-90-6P, Methyl 6-bromocaproate 33305-77-0P 41236-09-3P
53871-85-5P 81393-85-3P 116052-88-1P 116052-89-2P 116052-94-9P
116366-32-6P 143841-34-3P 154024-64-3P 154024-65-4P 154024-67-6P
154024-68-7P 154024-69-8P 154024-72-3P, Biotinyl-D-alanine
154024-74-5P 154024-75-6P 154024-76-7P 167861-55-4P 167861-58-7P
167861-59-8P 167861-60-1P **167861-61-2P 167861-62-3P**
167861-73-6P 167861-74-7P 180737-49-9P **180737-51-3P**
180737-52-4P 180737-53-5P 180737-54-6P **180737-55-7P**
180737-56-8P 180978-51-2P 180978-52-3P 180978-53-4P
180978-54-5P 181065-46-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(diagnostic and therapeutic pretargeting methods using metal chelates)
- IT 64987-85-5D, SMCC, **conjugates** with avidin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiolabeled biotin **conjugate** pretargeting with; diagnostic
and therapeutic pretargeting methods using metal chelates)
- IT 154024-49-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(tumor cell targeting with avidin **conjugate** and; diagnostic
and therapeutic pretargeting methods using metal chelates)

L4 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:158255 CAPLUS

DOCUMENT NUMBER: 124:317848

TITLE: Benzenesulfonamide-peptide **conjugates** as probes for secondary binding sites near the active site of carbonic anhydrase

AUTHOR(S): Sigal, George B.; Whitesides, George M.

CORPORATE SOURCE: Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(5), 559-64

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Libraries of N-(4-sulfamoylbenzoyl)oligoglycines terminated with different L-amino acids were screened to identify tight binding inhibitors of human carbonic anhydrase II. Inhibitors terminated with hydrophobic amino acids showed significant enhancements in binding compared to the corresponding glycine derivs. No enhancements were observed due to polar interactions.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 7

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(benzenesulfonamide **conjugate**; preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT Combinatorial library

(peptide; preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT Molecular structure-biological activity relationship

(carbonate dehydratase-binding, preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 9001-03-0, Carbonic anhydrase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(human II; preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 143288-21-5 165682-39-3 165682-40-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT	165682-42-8P	165682-43-9P	176170-35-7P	176170-36-8P	
	176170-37-9P	176170-38-0P	176170-39-1P	176170-40-4P	176170-41-5P
	176170-42-6P	176170-43-7P	176170-44-8P	176170-45-9P	176170-46-0P
	176170-47-1P	176170-48-2P	176170-49-3P	176170-50-6P	176170-51-7P
	176170-52-8P	176170-53-9P	176170-54-0P	176170-55-1P	176170-56-2P
	176170-57-3P	176170-58-4P	176170-59-5P	176170-60-8P	176170-61-9P
	176170-62-0P	176170-63-1P	176170-64-2P	176170-65-3P	176170-66-4P
	176170-67-5P	176170-68-6P	176170-69-7P	176170-70-0P	176170-71-1P
	176170-72-2P	176170-73-3P	176170-74-4P	176170-75-5P	176170-76-6P
	176170-77-7P	176170-78-8P	176170-79-9P	176170-80-2P	176170-81-3P
	176170-82-4P	176170-83-5P	176170-84-6P	176170-85-7P	176170-86-8P
	176170-87-9P	176170-88-0P	176170-89-1P	176170-90-4P	176170-91-5P
	176170-92-6P	176170-93-7P	176170-94-8P	176170-95-9P	176170-96-0P
	176170-97-1P	176170-98-2P	176170-99-3P	176171-00-9P	176171-01-0P
	176171-02-1P	176171-03-2P	176171-04-3P	176171-05-4P	176171-06-5P

176171-07-6P 176171-08-7P 176171-09-8P 176171-10-1P
 176171-11-2P 176171-12-3P 176171-13-4P 176171-14-5P 176171-15-6P
 176171-16-7P 176171-17-8P 176171-18-9P
 176171-19-0P 176171-20-3P 176171-21-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 56-40-6, Glycine, reactions 56-41-7, L-Alanine, reactions 56-45-1, Serine, reactions 56-84-8, Aspartic acid, reactions 56-85-9, Glutamine, reactions 56-86-0, Glutamic acid, reactions 61-90-5, Leucine, reactions 63-68-3, Methionine, reactions 63-91-2, L-Phenylalanine, reactions 70-47-3, Asparagine, reactions 72-18-4, Valine, reactions 72-19-5, Threonine, reactions 73-32-5, Isoleucine, reactions 74-79-3, L-Arginine, reactions 138-41-0 147-85-3, Proline, reactions 327-57-1, Norleucine 943-80-6, p-Amino-L-phenylalanine 949-99-5, p-Nitro-L-phenylalanine 1132-68-9, p-Fluoro-L-phenylalanine 6230-11-1, O-Methyltyrosine 14173-39-8, p-Chloro-L-phenylalanine 20859-02-3, L-tert-Leucine 58438-03-2, 3-(2-Naphthyl)-L-alanine

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

IT 67460-24-6P 154715-61-4P 176170-33-5P 176170-34-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and carbonic anhydrase active side binding of benzenesulfonamide-peptide **conjugates**)

L4 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:966994 CAPLUS

DOCUMENT NUMBER: 124:176877

TITLE: Synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their properties

AUTHOR(S): Nogusa, Hideo; Yano, Toshiro; Okuno, Satoshi; Hamana, Hiroshi; Inoue, Kazuhiro

CORPORATE SOURCE: Drug Delivery System Inst., Ltd., Chiba, 278, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1995), 43(11), 1931-6

CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The amino group of doxorubicin (DXR) was found to be bound to the carboxyl group of carboxymethylpullulan (CMPul) either directly or through tetrapeptide spacers, including Gly-Gly-Phe-Gly, Gly-Phe-Gly-Gly and Gly-Gly-Gly-Gly. These conjugates had DXR contents of 6.1-7.1%, with the degree of substitution of carboxymethyl groups being 0.6 per sugar moiety. These conjugates associate in phosphate-buffered saline (PBS) (pH 7.4), forming micelles with hydrophobic DXR inside and hydrophilic CMPul on the outside. The amts. of DXR released from the conjugates in the presence of rat liver lysosomal enzymes were determined by HPLC. The rate of drug release differed among the conjugates tested. CMPul-DXR conjugate bound through Gly-Gly-Phe-Gly released 35% of its DXR over 24 h. On the other hand, CMPul-DXR conjugate without spacer released no free DXR. The antitumor effect of each conjugate in rats bearing Walker 256 was studied by monitoring the tumor wts. after a single i.v. injection. Compared with DXR, CMPul-DXR conjugates bound through Gly-Gly-Phe-Gly and Gly-Phe-Gly-Gly spacers significantly suppressed the tumor growth, while CMPul-DXR conjugate bound through Gly-Gly-Gly-Gly showed less antitumor

effect than DXR. CMPul-DXR conjugate without spacer showed no in vivo antitumor effect even at a dose equivalent to as much as 20 mg/kg of DXR.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 33

ST peptide carboxymethylpullulan doxorubicin **conjugate** prepn
antitumor; pullulan carboxymethyl **conjugate** prepn antitumor

IT Neoplasm inhibitors

(synthesis of carboxymethylpullulan-peptide-doxorubicin
conjugates and their antitumor activities)

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(**conjugates**, synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT Molecular structure-biological activity relationship

(neoplasm-inhibiting, synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 23214-92-8DP, Doxorubicin, reaction products with sodium carboxymethylpullulan **161254-06-4DP**, reaction products with sodium carboxymethylpullulan **161254-07-5DP**, reaction products with sodium carboxymethylpullulan **161254-12-2DP**, reaction products with sodium carboxymethylpullulan

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 79-11-8, reactions 556-50-3, Glycylglycine 721-90-4, Phenylalanylglycine 1738-82-5 3321-03-7, Glycylphenylalanine 9057-02-7, Pullulan 23214-92-8, Doxorubicin

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 79-11-8DP, reaction products with pullulan 5893-07-2P 9057-02-7DP, Pullulan, reaction products with chloroacetic acid, sodium salt 17293-97-9P 76378-71-7P **161254-06-4P** 161254-07-5P 161254-12-2P **173723-56-3P** 173723-57-4P **173723-58-5P** 173723-59-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

IT 104095-57-0P 161254-11-1P **161254-16-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis of carboxymethylpullulan-peptide-doxorubicin **conjugates** and their antitumor activities)

L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:795164 CAPLUS

DOCUMENT NUMBER: 123:225940

TITLE: Pretargeting methods and compounds comprising radiometal labeled biotin and biotin- or streptavidin-antibody **conjugates**

INVENTOR(S): Yau, Eric K.; Theodore, Louis J.; Gustavson, Linda M.

PATENT ASSIGNEE(S): Neorx Corp., USA

SOURCE: PCT Int. Appl., 180 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

Russel 09/674,526

FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9515335	A2	19950608	WO 1994-US13485	19941122
WO 9515335	A3	19950720		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6022966	A	20000208	US 1993-156565	19931122
EP 736035	A1	19961009	EP 1995-910066	19941122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09505831	T2	19970610	JP 1995-515670	19941122
PRIORITY APPLN. INFO.:			US 1993-156565	A 19931122
			US 1992-895588	A2 19920609
			US 1992-995381	B2 19921223
			WO 1993-US5406	A2 19930607
			WO 1994-US13485	W 19941122

AB Methods, compds., compns. and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin, as well as related compds., are described. Articles of manufacture useful in pretargeting methods are also discussed. In example, 186Re-chelated biotin and biotinylated monoclonal antibody to human colon tumor (NR-LU-10) were prepared and used in combination with avidin were performed in a 3-step pretargeting protocol in nude mice implanted with human colon tumor xenografts, and a enhanced tumor uptake of 186Re-chelated biotin in the presence of biotinylated antibody and avidin was observed. Also, streptavidin-NR-LU-10 conjugates were prepared and used in combination with 186Re-chelated biotin and asialoorosomucoid clearing agent (preparation described) for two-step pretargeting protocol experiment

IC ICM C07K001-08

CC 15-3 (Immunochemistry)

Section cross-reference(s): 8, 34, 63

ST radiometal biotin **conjugate** biotinylated antibody; streptavidin monoclonal antibody **conjugate** tumor targeting

IT Orosomucoids

RL: MOA (Modifier or additive use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(asialo-; **conjugates**; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Radioelements, biological studies

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(metal; chelate; **conjugates**; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Neoplasm

(pretargeting; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

IT Metals, biological studies

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(radio-; chelate; **conjugates**; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in

- pretargeting method for tumor diagnosis and therapy)
- IT Neoplasm inhibitors
(radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Intestine, neoplasm
(colon, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Albumins, biological studies
RL: MOA (Modifier or additive use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates**, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Antibodies
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**conjugates**, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Avidins
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**conjugates**, radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Antibodies
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(monoclonal, **conjugates**; radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Peptides, reactions
RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(tetra-, acyclic; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Amides, reactions
RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(tetra-, cyclic; radiometal labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT Peptides, reactions
RL: MOA (Modifier or additive use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(tri-, acyclic; radiometal-labeled biotin and **conjugates** of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT 59-23-4D, Galactose, albumin **conjugates** 9004-54-0, Dextran, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as clearing agent; radiometal-labeled biotin and **conjugates**

- of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT 9013-20-1P, Streptavidin
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)
 (conjugates; radiometal-labeled biotin and conjugates
 of antibody and biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT 56602-33-6
 RL: MOA (Modifier or additive use); USES (Uses)
 (radiometal-labeled biotin and conjugates of antibody and
 biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT 60-32-2, 6-Aminocaproic acid 107-97-1, N-Methylglycine 949-99-5
 2389-60-8 3655-05-8 4224-70-8, 6-Bromocaproic acid 31954-27-5
 167861-71-4 167861-72-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (radiometal-labeled biotin and conjugates of antibody and
 biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT 556-33-2P, Triglycine 2780-89-4P, Methyl 6-aminocaproate 14273-90-6P,
 Methyl 6-bromocaproate 28320-73-2P 33305-77-0P 35013-72-0P
 41236-09-3P 53871-85-5P 53906-36-8P 62222-21-3P 69705-14-2P
 81393-85-3P 87548-77-4P 116052-89-2P 116366-32-6P 123317-52-2P
 135825-00-2P 143841-34-3P 154024-43-8P 154024-45-0P 154024-64-3P
 154024-65-4P 154024-67-6P 154024-68-7P 154024-75-6P 154024-76-7P
 167861-56-5P 167861-58-7P 167861-59-8P 167861-60-1P
 167861-61-2P 167861-62-3P 167861-63-4P
 167861-64-5P 167861-65-6P 167861-66-7P 167861-68-9P
 167861-69-0P 167861-73-6P 167861-74-7P 167861-75-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (radiometal-labeled biotin and conjugates of antibody and
 biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT 154024-42-7P 167861-67-8P 167861-70-3P 167861-76-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)
 (radiometal-labeled biotin and conjugates of antibody and
 biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)
- IT 14133-76-7DP, Technetium-99, complexes with chelate-biotin
 conjugate, biological studies 14998-63-1DP, Rhenium-186,
 complexes with chelate-biotin conjugate, biological studies
 60239-18-1DP, 1,4,7,10-Tetraazacyclododecane-N,N',N'', N'''-tetraacetic
 acid, derivs.; complexes; conjugates 123317-51-1DP, complexes;
 conjugates 154024-46-1DP, rhenium-186 and technetium-99
 complexes 154024-46-1P 167861-53-2DP, rhenium-186 and technetium-99
 complexes 167861-53-2P 167861-54-3DP, rhenium-186 and technetium-99
 complexes 167861-54-3P 167861-55-4DP, rhenium-186 and technetium-99
 complexes 167861-55-4P 167861-57-6DP, iodine labeled
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (radiometal-labeled biotin and conjugates of antibody and
 biotin or streptavidin in pretargeting method for tumor diagnosis and therapy)

Russel 09/674,526

ACCESSION NUMBER: 1995:386032 CAPLUS
DOCUMENT NUMBER: 122:299074
TITLE: Polysaccharide derivative and drug **carrier**
INVENTOR(S): Nogusa, Hideo; Hamana, Hiroshi; Yano, Toshiro; Kajiki, Masahiro; Yamamoto, Keiji; Okuno, Satoshi; Sugawara, Shuichi; Kashima, Nobukazu; Inoue, Kazuhiro
PATENT ASSIGNEE(S): Drug Delivery System Institute, Ltd., Japan
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9419376	A1	19940901	WO 1994-JP322	19940228
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2134348	AA	19940827	CA 1994-2134348	19940228
EP 640622	A1	19950301	EP 1994-907702	19940228
EP 640622	B1	20000809		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 195324	E	20000815	AT 1994-907702	19940228
ES 2149867	T3	20001116	ES 1994-907702	19940228
PT 640622	T	20001130	PT 1994-94907702	19940228
US 5688931	A	19971118	US 1994-325296	19941228
GR 3034416	T3	20001229	GR 2000-402104	20000918
PRIORITY APPLN. INFO.:			JP 1993-38635	A 19930226
			WO 1994-JP322	W 19940228
AB	A novel polysaccharide derivative [e.g. sodium carboxymethyl pullulan-3'-N-(Gly-Gly-Phe-Gly)-doxorubicin] is prepared and a drug carrier and a drug composite both comprise said derivative. The derivative is a carboxylated polysaccharide wherein a peptide chain composed of one to 8 same or different amino acids is introduced into part or all of the carboxyl groups of the polysaccharide and wherein part or all of those amino or carboxyl groups of the peptide chain which do not participate in the above linkage to the carboxyl groups of the polysaccharide may be bonded to the carboxyl, amino or hydroxyl groups of another compound (e.g. a drug) through amide or ester bonds. The derivative can migrate to the tumor-bearing region so readily that it can efficiently send drugs which are problematic in the side effects or have limited persistence of the drug activity in the tumor-bearing region.			
IC	ICM C08B037-00			
CC	63-6 (Pharmaceuticals)			
	Section cross-reference(s): 1			
ST	polysaccharide deriv prepn drug carrier			
IT	Neoplasm inhibitors			
	Pharmaceutical dosage forms			
	(preparation of polysaccharide derivative as drug carrier)			
IT	Polysaccharides, biological studies			
	RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)			
	(preparation of polysaccharide derivative as drug carrier)			
IT	5893-05-0 9057-02-7, Pullulan 9064-52-2 9067-32-7, Hyaluronic acid sodium salt 23214-92-8D, Doxorubicin, derivs. 39422-83-8, Sodium carboxymethyl dextran 64859-64-9 76378-71-7 104095-57-0 105156-94-3 161254-03-1 161254-04-2 161254-06-4 161254-08-6 161254-11-1 161254-13-3 161254-15-5 161254-16-6 163254-82-8			

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of polysaccharide derivative as drug carrier)
 IT 109116-58-7DP, reaction products with doxorubicin derivs. 109116-58-7P
 161254-05-3P 161254-07-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of polysaccharide derivative as drug carrier)
 IT 23214-92-8, Doxorubicin
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT
 (Reactant or reagent); USES (Uses)
 (preparation of polysaccharide derivative as drug carrier)
 IT 9064-52-2DP, reaction product with doxorubin derivs. 9067-32-7DP,
 reaction product with doxorubin derivs. 39422-83-8DP, Sodium
 carboxymethyl dextran, reaction product with doxorubin derivs.
 64859-64-9DP, reaction product with doxorubin derivs. 105156-94-3DP,
 reaction product with doxorubin derivs. 147513-69-7DP, reaction product
 with polysaccharides 147513-69-7P 161254-03-1DP, reaction product with
 polysaccharides 161254-05-3DP, reaction product with polysaccharides
 161254-07-5DP, reaction product with polysaccharides 161254-09-7P
 161254-10-0DP, reaction product with polysaccharides 161254-10-0P
 161254-12-2DP, reaction product with polysaccharides 161254-12-2P
 161254-14-4DP, reaction product with polysaccharides 161254-14-4P
 163254-82-8DP, reaction product with doxorubin derivs.
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of polysaccharide derivative as drug carrier)
 IT 161254-06-4DP, reaction product with polysaccharides
 161254-09-7DP, reaction product with polysaccharides
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (preparation of polysaccharide derivative as drug carrier)

L4 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:490207 CAPLUS

DOCUMENT NUMBER: 119:90207

TITLE: Synthesis, metal chelate stability studies, and enzyme
 digestion of a peptide-linked DOTA
 derivative and its corresponding radiolabeled
 immunoconjugates

AUTHOR(S): Li, Min; Meares, Claude F.

CORPORATE SOURCE: Dep. Chem., Univ. California, Davis, CA, 95616-0935,
 USA

SOURCE: Bioconjugate Chemistry (1993), 4(4), 275-83
 CODEN: BCCHES; ISSN: 1043-1802

DOCUMENT TYPE: Journal

LANGUAGE: English

AB By directly coupling a tetrapeptide to DOTA through an amide bond, a novel
 DOTA derivative, DOTA-glycylglycylglycyl-L-p-nitrophenylalanine amide, was
 synthesized. This new precursor bifunctional chelating agent was
 converted to DOTA-glycylglycylglycyl-L-p-isothiocyanatophenylalanine and
 conjugated to monoclonal antibody Lym-1. Serum stability studies show
 that the radiolabeled conjugates are kinetically inert under physiol.
 conditions. The rates of loss of radiometals in human serum are 0.1% per
 day for In³⁺, 0.02% per day for Y³, and 0.3% per day for Cu²⁺-labeled
 immunoconjugates. In the presence of the liver enzyme cathepsin B, an in
 vitro digestion of ¹¹⁴mIn-labeled conjugate yields a small fragment containing
¹¹⁴mIn. Characterization of the cleavage products shows that this liver
 enzyme hydrolyzes the peptide linkage before the phenylalanine residue,
 freeing the In-DOTA-triglycine complex from the conjugate. However, the
 liver enzyme cathepsin D does not cleave the linkage over the span of 7
 days.

- CC 8-9 (Radiation Biochemistry)
- IT Antibodies
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (monoclonal, **conjugates**, with radiometals and peptide-linked DOTA derivative, preparation and stability and enzyme digestion of)
- IT 149226-84-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and coupling with DOTA)
- IT 13982-36-ODP, Yttrium-88, DOTA derivative-monoclonal antibody **conjugates** 15757-86-5P, Copper-67, preparation 149206-87-1DP, radiometal-monoclonal antibody **conjugates**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and stability and enzyme digestion of)
- IT 13981-55-ODP, Indium-114, DOTA derivative-monoclonal antibody **conjugates**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and stability and enzyme digestion of metastable)
- IT 149206-85-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and trifluoroacetylation of)
- IT 9025-26-7, Cathepsin D 9047-22-7, Cathepsin B
 RL: BIOL (Biological study)
 (radiometal-DOTA derivative-monoclonal antibody **conjugate** digestion by)

L4 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1984:412062 CAPLUS
 DOCUMENT NUMBER: 101:12062
 TITLE: Enzymic cleavage of side chains of soluble polymers
 AUTHOR(S): Labsky, Jiri; Mikes, Frantisek
 CORPORATE SOURCE: VSCHT, Prague, Czech.
 SOURCE: Sbornik Vysoke Skoly Chemicko-Technologicke v Praze,
 S: Polymery--Chemie, Vlastnosti a Zpracovani (1983),
 S 9, 279-308
 CODEN: SVSZD5; ISSN: 0139-908X
 DOCUMENT TYPE: Journal
 LANGUAGE: Czech

AB Models were prepared for the study of release rates of biol. active substances (drugs, hormones, inhibitors, or enzymes) covalently bound to soluble organic polymers after endocytosis and exposure to liposomal hydrolases.

Soluble polymers, polymethacrylates or poly(hydroxypropylmethacrylamides) with d.p. 25-30, bound by amide bonds with L-phenylalanyl nitroanilides through spacers of variable length and structure (peptides or aliphatic chains) were used as carriers. Chymotrypsin [9004-07-3]-catalyzed hydrolysis rates of the C-terminal anilide bonds were correlated with the length and structure of the spacers and the structure of the anilide groups. Steric conditions for the interactions of the spacer chains with chymotrypsin active site and affinity site are discussed.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 7, 34

ST chymotrypsin hydrolysis polymethacrylate peptide anilide; drug **carrier** polymer

IT Pharmaceuticals

(**carriers** for, phenylalanyl nitroanilide methacrylate polymers as models of)

IT 57950-58-0P 57950-81-9P 61435-96-9P 61435-97-0P **61435-98-1P**
 61435-99-2P 61436-00-8P 62238-85-1P 64129-74-4P 64129-75-5P

64134-54-9P	64651-29-2P	70587-66-5P	70587-67-6P	70587-68-7P
71187-45-6P	73807-80-4P	73814-11-6P	90409-02-2P	90409-03-3P
90409-04-4P	90409-05-5P	90409-06-6P	90409-07-7P	90409-08-8P
90409-09-9P	90409-10-2P	90409-12-4P	90409-14-6P	90409-16-8P
90409-18-0P	90409-20-4P	90409-22-6P	90409-24-8P	90409-26-0P
90409-28-2P	90409-30-6P	90409-32-8P	90409-34-0P	90409-36-2P
90409-38-4P	90409-40-8P	90409-42-0P	90409-44-2P	90409-46-4P
90409-48-6P	90409-50-0P	90409-52-2P	90409-54-4P	90409-56-6P
90409-58-8P	90409-60-2P	90409-62-4P	90409-65-7P	90409-66-8P
90409-67-9P	90409-68-0P	90409-69-1P	90409-70-4P	90409-71-5P
90409-72-6P	90409-73-7P	90409-74-8P	90409-76-0P	
90426-73-6P	90426-75-8P	90426-77-0P		

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and chymotrypsin hydrolysis of, biomols. and drug release in relation to)

L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1980:501418 CAPLUS

DOCUMENT NUMBER: 93:101418

TITLE: Degradation of side chains of N-(2-hydroxypropyl)methacrylamide copolymers by lysosomal enzymes

AUTHOR(S): Duncan, Ruth; Lloyd, John B.; Kopecek, Jindrich
CORPORATE SOURCE: Dep. Biol. Sci., Univ. Keele, Keele/Staffordshire, ST5 5BG, UK

SOURCE: Biochemical and Biophysical Research Communications (1980), 94(1), 284-90
CODEN: BBRCA9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 22 N-(2-hydroxypropyl)methacrylamide copolymers, each containing a different, potential degradable side chain, were incubated with rat liver tritosomes. Four of the side chains were digestible as judged by the liberation of a terminal 4-nitroaniline residue. The pH optimum for the degradation of the side chain -ε-aminocaproyl-phenylalanyl-4-nitroanilide was in the range 5.75-6.5 over the first hour of incubation and somewhat lower (pH 5.5-6.0) after this time. The degradation of the above side chain had a Km value of 58.3 mg/mL. The use of these compds. as drug carrier mols. is discussed.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 7, 34, 35

ST hydroxypropylmethacrylamide copolymer degrading lysosome enzyme; drug carrier hydroxypropylmethacrylamide copolymer; methacrylamide copolymer drug carrier

IT 53282-69-2DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 66493-40-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74541-62-1DP, reaction products with oligopeptides, nitrophenylamino containing 74569-67-8DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74569-69-0DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74569-71-4DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74588-99-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-00-7DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-01-8DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-02-9DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-03-0DP,

reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-04-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-05-2DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-06-3DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-07-4DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-08-5DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-09-6DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-10-9DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-11-0DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-12-1DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-13-2DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-14-3DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers 74589-15-4DP, reaction products with N-(hydroxypropyl)methacrylamide-methacrylamide copolymers

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and degradation of, by lysosomal enzymes, drug carrier in relation to)

=>